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WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. No. 167. **Public Health Nursing. Fourth Report of the Expert Committee on Nursing.** Geneva, 6–11 October 1958. 31 pp. 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

In its 3 previous reports the World Health Organization Expert Committee on Nursing dealt mainly with nursing education and administration. Reference only was made in these reports to public health nursing but its 4th session held in Geneva from 6 to 11 October 1958, "was called to give more detailed and specific consideration to the functions of public health nursing, the administration of public health nursing services, and education for public health nursing".

The report of the committee's deliberations at this 4th session is here presented. It has sections with many sub-sections on functions, administration, education, research and recommendations in the wide field of public health nursing.

Among the recommendations are: (1) that "WHO should undertake or sponsor inter-country research and studies of methods of evaluation of public health nursing services", (2) the convening of an expert committee to discuss the role and preparation of the auxiliary worker in public health nursing should be considered by WHO, (3) that national and regional planning be promoted to develop appropriate facilities for "post-basic and advanced education for public health nursing", (4) that there should be research in and critical consideration of current methods for the identification, selection and training of those in positions of leadership in the field of public health nursing, and (5) "the convening of regional and national seminars or conferences to consider the findings of this report with particular reference to their local application".

M. E. Delafield

CARTWRIGHT, Ann & JEFFERYS, Margot. **Married Women who Work: Their Own and their Children's Health.** *Brit. J. Preventive & Social Med.* 1958, Oct., v. 12, No. 4, 159–71.

This investigation was carried out in a new housing estate near London with a population of about 17,000 consisting mainly of young couples and their children. The data were obtained by means of interviews with the women themselves, from the records of general practitioners and schools and from reports made by health visitors and teachers. 40% of the married women were gainfully employed—18% full-time, 17% part-time and 5% were doing paid work at home. Whether women took up employment was found to be related to their age, to the number of children in their family and to the age of their youngest child. Very few mothers having a child under 2 years went out to work, about one-sixth of those with a child between 2 and 5 years were working—mostly part-time, but where the youngest child had reached school-age, about one-half of the mothers had obtained employment. The peak was reached where the youngest child was of secondary school age (11 to 15 years) when two-thirds of the mothers were at work. Thereafter, as the children left school and entered employment the proportion of mothers working declined.

Schoolchildren whose mothers were working had no more reported illness than those whose mothers were at home. Comparisons of the prevalence of such habits as bed-wetting, nail-biting and thumb-sucking did not suggest that the children of working mothers were adversely affected emotionally, nor were they of inferior stature to their age-mates whose mothers were not at work. Children of working mothers had less sickness absence from school, which may have been due to their making a relatively earlier return after illness. Assessments by health visitors and teachers did not suggest that the standards of child care were less satisfactory among the employed mothers. On the contrary, the teachers' reports showed that rather more of the children of working mothers were particularly well cared for. This could be attributed to the relative prosperity of their families. Personality ratings of the children showed little difference in self-confidence and sociability between those whose mothers did, and did not, work; cooperativeness was rated higher among the children of part-time workers, while perseverance and conscientiousness were rated somewhat lower in the children of full-time workers. The children of working mothers were seen less often by the general practitioners but were admitted to hospital rather more frequently than those whose mothers were not at work.

Attention was also given to the health and the use of services of the mothers themselves. Among the women under 45, those at work had a higher consultation rate with the general practitioners than those who did not but who had a similar number of children. Quite apart from whether they were employed or not, women with fewer children consulted their doctors more often than those with more children. Factors which may have influenced the consultation rates of these married women are discussed and the authors conclude that there was little difference between the health of women who worked and those who did not.

[See also DOUGLAS & BLOMFIELD, this *Bulletin*, 1959, v. 34, 511.] *S. P. W. Chave*

Maternal and Child Health

MINISTRY OF HEALTH. **Report of the Maternity Services Committee** [CRANBROOK, Chairman]. pp. vi + 125. 1959. London: H.M. Stationery Office. [6s. 6d.]

The Maternity Committee derives from evidence given to the Guillebaud Committee on the cost of the National Health Service [this *Bulletin*, 1956, v. 31, 1053] to the effect that the tripartite administration of the National Health Service caused special weaknesses in the Maternity Services. The Guillebaud Committee contained no medical member and they recommended that the organization of maternity services should be reviewed by a special committee. This special committee was set up in April 1956 under the chairmanship of the Earl of Cranbrook. It contained 11 other members, of whom 6 were medical and 2 nursing.

Those who desire a complete re-organization of the service under a single authority will be disappointed as the committee recommend unanimously that the present tripartite structure should remain but "with a clearer definition of the responsibilities of the [3] respective bodies".

Apart from consideration of this major principle the main points of controversy were (1) how much domiciliary midwifery is likely to be needed in the future, and as a corollary how many hospital beds are needed, and (2) whether every registered doctor should be entitled to participate in the national maternity scheme and be paid for his services.

Institutional confinements were 15% of the total births in 1927; 24% in 1932; 39·7% in 1937; 50% in 1946 and 64·6% in 1957. A more careful selection of patients for either domiciliary or institutional confinement is advocated and it is concluded that, as a national percentage, institutional confinements should be about 70. But additional beds for ante-natal cases will be required: the estimated number is between 20 and 25% of all confinements. To provide these and to raise hospital deliveries to 70% will mean either more maternity beds or reducing the average length of stay.

Any drastic reduction in the latter should not be countenanced and the patient should remain normally in hospital for 10 days after delivery.

On the other main issue it is stated that "There is not enough domiciliary maternity work available to enable every general practitioner to obtain and maintain the necessary standard of skill". The committee repudiate the claim of some witnesses that as every registered medical practitioner has been trained, and passed an examination, in obstetrics he should be entitled, if he so desires, to attend maternity cases under the National Health Service and to special fees. The committee recommend that the special obstetric list should be continued and that the qualifications for admission to it should be tightened. A 6 months' resident appointment in an obstetric unit should be the normal criterion for admission to the list: retention on it should be reviewed every 3 years and the name should be removed of anyone who has booked fewer than 60 cases in the preceding 3 years and has not attended the deliveries in at least 30. All the general practitioner obstetricians should have access to beds in general practitioner hospitals and the new maternity beds required should be available for the patients of general practitioner obstetricians and attended by them.

The report contains many other points of interest. A table gives the maternal mortality rates (including abortion) for 1955 in a number of countries: that of England and Wales, 0·7 per 1,000 live births, is exceeded only by Canada, 0·8, and the lowest is New Zealand, 0·4. The 1957 rate (excluding abortions) for England and Wales was 0·39 per 1,000 live and stillbirths. It is the lowest ever recorded and compares with 3·56 in 1931–5.

There is a serious shortage of practising midwives. The importance of ante-natal care is emphasized throughout the report. Local authority ante-natal clinics should continue and be staffed on the medical side by general practitioner obstetricians rather than by assistant medical officers of health who do not attend deliveries.

"Co-ordination" and "Co-operation" are words somewhat overworked nowadays and they appear often in this report. Detailed suggestions for making them effective in the maternity service are made.

The report is courageous in its recommendations about the general practitioner obstetrician list, but otherwise the main theme is that the present system works reasonably well but it can and should be improved in detail. *Allen Daley*

MELLIN, G. W. & KENT, Mary P. **Ophthalmia Neonatorum. Is Prophylaxis Necessary?** *Pediatrics.* Springfield, Ill. 1958, Nov., v. 22, No. 5, 1006–15. [40 refs.]

In 1956 the Sanitary Code of New York City which required that prophylactic measures against ophthalmia

neonatorum should be undertaken at birth was repealed. The reason for this repeal was mainly the introduction of sulphonamides and antibiotics, which are very effective therapeutic agents. This change in the law has been regarded as a scientific experiment which should be watched for a few years.

This paper describes observations made at the Sloane Hospital for Women in the period from April 1957 to October 1957 during which the routine prophylaxis with 1% silver nitrate was discontinued in all the delivery rooms. In this period the incidence and severity of discharging eyes decreased. Many of the reactions appear to have been of the mild type referred to in the literature as "sticky eyes" and only 4 were sufficiently severe to be regarded as ophthalmia neonatorum. The overall incidence of discharging eyes among the 1,974 infants observed in the 6 nurseries of the hospital was 64 (3·2%). This incidence was analysed and tables set out the frequencies of discharging eyes by post-partum day of onset, by nursery, by month and by weight of infant. The different bacteria isolated from discharging eyes are also recorded in a table with a comparison of those isolated from controls. In 4 infants *Neisseria gonorrhoeae* was isolated from the ocular discharge. The observations are fully discussed and compared with previous experience.

This incidence of 4 cases of gonorrhoeal ophthalmia neonatorum represents a marked increase over the 10 cases which had occurred in the previous 25 years, and for this reason "It has seemed expedient to continue prophylaxis" at present in the Medical Center.

M. E. Delafield

MINISTRY OF EDUCATION. **The Health of the School Child. Fifty Years of the School Health Service. Report of the Chief Medical Officer of the Ministry of Education for the Years 1956 and 1957** [CHARLES, J.]. 220 pp., illustrated. 1958. London: H.M. Stationery Office. [10s. 6d.]

This is the Report of the Chief Medical Officer of the Ministry of Education on the health of the school child for the years 1956 and 1957. The School Health Service completed its first 50 years of work in December 1957 and in this, the thirty-ninth in the series of reports, there is much valuable and interesting information with discussions on the development of the service as well as on the changed pattern of disease in the school child. The whole subject is dealt with in 21 chapters which contain much detailed description, many tables of numerical data and some good photographs.

Compared with children of 50 years ago boys and girls of today have much better physique and the expectation of life at birth is 20 years longer. Of every 1,000 children medically examined in the early days of the service 140 were verminous, 130 undernourished, 100 had defective footwear, 50 had inadequate clothing, 40 had rickets and 30 had heart disease. In 1957 the figures per 1,000 were 40 verminous, 17 were of unsatisfactory physical condition, 2 had heart disease and none had rickets. The ravages of infectious disease have been greatly restricted, as for example: scarlet fever in 1901–10 caused 271 deaths annually in every million children under 15 years of age but no deaths in 1957; whooping cough 815 in 1901–10 and 8 in 1957; and measles 915 in 1901–10 and 9 in 1957. Diphtheria caused no deaths in 1957 as compared with 571 per million in 1901–10 and 1,122 in 1861–70. In spite of these improvements there is no ground for complacency since many problems have to be considered, among which are mentioned the fact that 2,000 children contract tuberculosis annually, the high accident and violent-death rate, the incidence of physical defects found on entry to school which is about 15%, the increased amount of dental decay, the frequency of otitis media and the high tonsillectomy rate.

The first chapter of the report describes the development of the Health Service and its scope in 1957. This is followed by chapters on handicapped children and on the findings at medical inspection and the results of treatment with much general and clinical information. School dentistry during 50 years and the dental service of today are described. Other separate chapters include those which deal with growth and nutrition, visual defects, defective hearing, physically handicapped children, educationally sub-normal children, the child guidance service, tuberculosis in the school, food poisoning, accidents in childhood and health education. The differing findings at periodic medical inspections are described in a separate chapter. These differences may be extreme, as, for example, the prevalence of visual defects was found to range from 86 per 1,000 inspections in Salop to 9·6 in Devon, the incidence of skin conditions ranged from 21·8 in Wiltshire to 1·3 in Buckinghamshire and heart defects from 6·6 in Nottinghamshire to 0·2 in Leicestershire. There is discussion of the possible relation of these differences to heredity, environment, problems of recording or observer decision. The incidence of tonsillectomy in children is considered separately with much numerical information which shows its great geographical variation. The overall tonsillectomy rate of leavers was 20·9% but the range in different areas was extreme, *e.g.* in counties the percentage rate was 4·7 in Westmorland, 30 in Devon, 30·8 in London and 31·1 in East Sussex.

This is an admirable report. *M. E. Delafield*

ROXBURGH, R. C. & HAAS, L. **The Diagnostic Importance of Glycosuria in Lead Poisoning in Childhood.** *Arch. Dis. in Childhood.* 1959, Feb., v. 34, No. 173, 70–73. [22 refs.]

Glycosuria has frequently been reported as an incidental finding in cases of lead poisoning. It is the purpose of the present paper "to show the diagnostic value of glycosuria, especially in the cases of lead poisoning without encephalopathy". In the 3 cases which are reported here "it was the presence of marked glycosuria in the absence of a raised blood sugar level that led to a search for other evidence of lead poisoning".

The first case was in a boy aged 1½ years admitted with a 2-week history of malaise, vomiting, marked anorexia, severe constipation and loss of weight. He was very pale and listless. The chief findings were that the urine showed a moderate amount of sugar and blood haemoglobin was 50%. These observations led

to the suspicion of lead poisoning and further investigations revealed marked punctate basophilia of the red blood cells, dense heavy metal bands in radius and ulna on X-ray examination, increase in urinary coproporphyrins and a urinary lead concentration of 0·56 mgm. per litre. On questioning the parents they confirmed that the child had for 3 months been in the habit of chewing the paint off the edges of window-sills and doors. This paint was found to have a high lead content.

The second case in a girl aged 6¼ years was similar in that glycosuria raised the suspicion of lead poisoning which was confirmed by the appearance of the red blood cells, by X-ray and great increase in coproporphyrins in the urine. The child's father was a house painter but no clear source of the lead poisoning was determined although she had had the pica habit at the age of 2 years.

The third patient, a boy aged 4 years 8 months, was the most severely ill. He was admitted in deep coma, and neurological evidence led to a diagnosis of rising intracranial pressure. From this condition he recovered fully after operation. In this patient also the presence of glycosuria led ultimately to the proof of a diagnosis of lead poisoning. The source of the lead appears to have been his yellow and orange crayons which were found to contain 5% of lead.

All 3 patients were given prolonged treatment with oral calcium di-sodium versenate, and made good recovery. *M. E. Delafield*

Care of Old Persons and the Chronically Ill

MACFIE, Mary. **The Work of Health Visitors in connection with Elderly People.** *Med. Officer.* 1959, Mar. 13, v. 101, No. 11, 147–9.

In 1956–7 a survey was made of a 5% sample of persons of pensionable age in Aberdeen (*Annual Report* MOH, Aberdeen, 1957). 1,005 unselected old people were studied and a list of their main requirements, which are set out in this paper in a table, shows that visits by health visitors were " both the commonest need and the commonest un-met need ". In 1958 a study was made of the 203 individuals (with some exceptions) who had been deemed to require visits. The results of this follow-up study are here described with several numerical tables. The main findings were that during the year each person had on average received over 6 visits and that health visitors had advised 89% of the old people on their physical health, 67% on points of mental health and 69% on social problems. In 5 out of every 6 instances the visitor's advice had been followed in whole or in part. Health visitors had also initiated many services for the elderly such as chiropody, home help, claiming of allowances and others. *M. E. Delafield*

COMMISSION ON CHRONIC ILLNESS [MAYO, L. W. Chairman] Vol. IV. **Chronic Illness in the United States.**

This book was reviewed on p. 591.

Vital Statistics and Epidemiology

KANELLAKIS, A. P. **Seasonal Swing in Mortality in England and Wales.** *Brit. J. Preventive & Social Med.* 1958, Oct., v. 12, No. 4, 197–203, 2 figs.

The seasonal distribution of deaths by age and for each of the numerically important causes of death are shown graphically for 1952–6. The age-groups with the most pronounced seasonal trend were 4 weeks to 1 year, 1–2 years and 75 and over. The diseases with the largest relative peaks were influenza, bronchitis and pneumonia, bronchiectasis, and asthma. Cancer had the smallest variations in mortality during the year. February was generally the month with the largest mortality and the chief exceptions to this trend were suicide, with a peak mortality in April, and accidents and violence among males with a maximum in December. The minimum mortality was generally recorded in the summer months of July to September and the only cause of death with a winter minimum was appendicitis. *W. J. Martin*

INTERNAT. DIGEST HEALTH LEGISLATION. 1958, v. 9, No. 4, 605–53. [27 refs.] **Notification of Communicable Diseases. A Survey of Existing Legislation.**

This is a survey of the legislation of about 50 countries on the notification of communicable diseases or other conditions. An appendix gives lists of the conditions which are notifiable, the number of which may vary between 10 and 70. Included among the references are particulars of the relevant legislation in these countries.

In the introduction the value and also the shortcomings of notification of disease are discussed with particular reference to the "incompleteness of notification, the varying definitions of the same disease, and differences in the lists of diseases notifiable in various countries". Variations exist even between different parts of the same country. "Nevertheless, a trend towards making notification more uniform is observable."

A section of the survey deals with the classes of diseases notifiable in different countries. In some countries there is a single undivided list whereas in others there are 2 or more classes as, for example, in the Belgian Congo where 6 classes of diseases are separately stated: quarantinable, epidemic, endemic, food poisoning, all other communicable or epidemic diseases and deficiency diseases in general.

The notification of carriers is given particular attention, for only 10 out of the 50 or more countries where legislation is examined in this survey require carriers to be notified. Other sections of the survey are entitled: "When notification must be made", "Who must make notification", and "To whom notification must be sent". *M. E. Delafield*

KAMAL, Ahmed Mohamed [D.P.H.], **Epidemiology of Communicable Diseases.**

This book was reviewed on p. 591.

Communicable Diseases

For the bacteriology of these diseases see the section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order: General; Diphtheria, Whooping Cough, Streptococcal Infections, Staphylococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis, Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Encephalitis; Enteric Fevers.

GAJDUSEK, D. C., ROGERS, Nancy G. & BANKHEAD, Annie S. **Serologic Survey of Viral and Rickettsial Diseases among Jungle Inhabitants of the Upper Amazon Basin. Presence during Infancy, Childhood and Adolescence of Antibodies to Rickettsiae, to Viruses of Poliomyelitis, Mumps, Herpes, PLV Group, Yellow Fever and to the Group B Arthropod-Borne Viruses.** *Pediatrics.* Springfield, Ill. 1959, Jan., v. 23, No. 1 Pt. 1, 121–31, 6 figs. [18 refs.]

Sera were obtained from individuals living in primitive jungle communities in the upper Amazon basin in 1955. The donors of serum had lived all their lives in the Peruvian or Bolivian jungle. Antibodies to all 3 types of poliovirus were acquired early in life; by 5 years 39 out of 42 children had antibodies to all 3 types. The maximum antibody levels were found at 5–9 years of age. One Bolivian aged 17 had no antibodies to polioviruses. None of the sera had antibodies to yellow fever virus, but it is pointed out that yellow fever has occurred in Southern Bolivia (*Pan American Sanitary Bureau. Scientific Publication No.* 19, 1955 [*Tropical Diseases Bulletin*, 1956, v. 53, 870]). Similarly no antibodies were found to EMC virus (encephalomyocarditis). 6 out of 85 sera reacted with group B Arbor viruses (Japanese B encephalitis). Antibodies to mumps and herpes simplex viruses were acquired early in life and the majority of adults had antibodies. Psittacosis-LGV antibodies were acquired by adolescents and adults, suggesting that lymphogranuloma venereum rather than ornithosis was the causal agent. A few sera reacted in low titre with Q fever antigen, but none with the epidemic or murine typhus antigens. *A. J. Beale*

COFFEY, Victoria P. & JESSOP, W. J. E. **Rubella and Incidence of Congenital Abnormalities.** *Irish J. Med. Sci.* 1959, Jan., 6th Ser., No. 397, 1–11. [14 refs.]

Questions to patients attending antenatal departments of 4 hospitals in Dublin revealed 26 cases of rubella during pregnancy and 49 of contact with the disease. The subsequent condition of the baby was noted at birth and again 3 months later. Of the infants of 10 mothers who were infected during the first trimester one miscarried, one had talipes equinovarus and one had a congenital cataract. Of the 30 who had been in contact during this interval but without clinical disease one had a baby with congenital heart disease. With 16 attacks later in pregnancy there were 2 affected infants (1 talipes equinovarus and 1 anencephaly) and with 19 contacts one case of talipes equinovarus. The

figures are presented in considerable detail [though not by actual month of pregnancy] and compared with a number of retrospective and prospective surveys from the literature. *A. Bradford Hill*

MILLEN, J. W. **Some Aspects of the Relationship between Environment and Congenital Malformations.** *Irish J. Med. Sci.* 1959, Jan., Sixth Ser., No. 397, 22–9. [55 refs.]

The author reviews the experimental work with laboratory animals showing the effects upon the production of malformed young both of the external environment, *e.g.* X-radiation, anoxia and hypothermia, and of the internal environment, *e.g.* maternal hypovitaminosis, administration of hormonal agents, trypan blue, etc. Only the fringe of the problems concerning the role of environment in the production of congenital malformations has yet been explored. In the development of a normal child a general balance of nutritional factors may well be required.

A. Bradford Hill

GITLIN, D.; GROSS, P. A. M.; JANEWAY, C. A. **The Gamma Globulins and their Clinical Significance. I. Chemistry, Immunology and Metabolism. II. Hypogammaglobulinemia** [GITLIN, GROSS & JANEWAY]. *New England J. of Med.* 1959, Jan. 1 & 8, v. 260, Nos. 1 & 2, 21–7; 72–6. **III. Hypergammaglobulinemia. IV. Therapeutic Uses of Gamma Globulins** [GROSS, GITLIN & JANEWAY]. *Ibid.*, Jan. 15 & 22, Nos. 3 & 4, 121–5; 170–8. [210 refs.]

I. Human gamma globulins constitute a broad band of serum protein molecules that migrate slowly during electrophoresis. They have differing isoelectric points and solubility constants but have immunologically common antigenic groups, and antibody prepared against a highly purified subfraction of gamma 2 globulin, for example, will cross-react with other subfractions in the broad gamma band. They should be regarded as populations of closely related substances. It seems fairly certain that they are synthesized in plasma cells and are then released into the extracellular body fluid. Their catabolic half life appears to be about 20 days and, in a person weighing 70 kgm., about 2·5 gm. would be synthesized and catabolized daily. Synthesis of gamma globulin can be accelerated by antigen stimulus and depressed by adrenal steroids. Catabolism is increased in idiopathic hypoproteinaemia and the nephrotic syndrome and gamma globulin is lost also in the removal of ascitic fluid, in haemorrhage and in oozing through skin, in burns in eczema or through an inflamed bowel wall.

II. There are at least 3 forms of agammaglobulinaemia: *congenital*, which occurs predominantly in males, with the first severe infection between 9 months and 2 years of age; *acquired*, which occurs in either sex, with onset at any time from childhood to old age; *transient* which occurs for a short time in early infancy. In the congenital form, infections are usually due to the pyogenic group and otitis and sinusitis, pneumonia, meningitis or pyoderma may occur repeatedly. The affected child seems to have some antiviral as compared with antibacterial immunity. Gamma globulin is never completely absent but is usually present at less than 50 mgm. per 100 ml. as compared with a normal plasma concentration of between 600 and 1,100 gm. per 100 ml. Antigenic stimulation, either through attempted immunization or by natural infection, does not lead to antibody formation, or to the formation of plasma cells by lymph nodes. The condition appears to be a hereditary disorder, occurring predominantly in males, and apparently transmitted as a sex-linked recessive characteristic. Acquired agammaglobulinaemia may be idiopathic or result from neoplastic invasion of lymphoid tissue. In the transient form there is a temporary delay in synthesis of gamma globulin. Sudden death in infancy may be due to overwhelming infection in such children. In the nephrotic syndrome the fall in the gamma globulin is due partly to the proteinuria and partly to increased catabolism.

III. Acute infections first produced a rise in alpha globulins: only when infection is prolonged is there a significant rise in gamma globulin. This occurs in chronic granulomata and in rheumatic fever. Raised gamma globulin is one of the commonest findings in liver disease: the highest levels occur in cirrhosis, moderate levels in toxic or viral hepatitis. Flocculation tests are related to disproportion in the serum protein fractions. Severe malnutrition, the collagen diseases and certain neoplasms, especially myeloma, show rises in gamma globulin in the serum. More than two-thirds of patients with sarcoidosis have hypergammaglobulinaemia.

IV. Gamma globulin has 3 therapeutic advantages over the parent plasma—it can be given in much less bulk, the gamma globulin being concentrated 25 times, it retains its potency much longer, and it is almost free from the danger of transmitting serum hepatitis. It is effective in preventing recurrent infections in all 3 forms of agammaglobulinaemia. Its use in the prophylaxis of measles and other virus diseases, including hepatitis and poliomyelitis, must be based on sound theory. Hyperimmune gamma globulin has been used with effect in the prophylaxis of smallpox and the treatment of various complications of vaccination. Its use in mumps, chickenpox, herpes zoster and simplex is more uncertain. [These 4 articles provide a scholarly review of the whole subject and can be highly recommended for careful study.] *A. B. Christie*

HAMMACK, W. J., BOLDING, F. Elna & FROMMEYER, W. B., Jr. **The Dysgammaglobulinemic Syndrome.** *Ann. Intern. Med.* 1959, Feb., v. 50, No. 2, 288–99, 9 figs. [19 refs.]

"Four patients with unusual susceptibility to infection and an associated abnormal serum gamma globulin peak of a discrete homogeneous nature are reported. Immunologically the serum proteins of three of the patients were related to myeloma proteins, and in one of the patients the serum protein was related to macroglobulin. However, within the limits of a three and one-half year observation period, the authors consider that the protein abnormality in these patients, who have shown

no evidence of classic myeloma, represents a new syndrome. Treatment has consisted of careful follow-ups and the use of antibiotics as soon as definite evidence of infection occurs."

HAVARD, C. W. H., GARROD, L. P. & WATERWORTH, Pamela M. **Deaf or Dead? A Case of Subacute Bacterial Endocarditis treated with Penicillin and Neomycin.** *Brit. Med. J.* 1959, Mar. 14, 688–9.

This case report poses a difficult question of clinical judgment.

A man of 47, after dilatation of a urethral stricture, suffered from subacute bacterial endocarditis with a ruptured aortic cusp. Treatment with penicillin, 1 mega unit every 6 hours, and streptomycin, 1 gm. twice daily, was given for 4 days, and thereafter penicillin alone, 2·5 mega units, with probenecid, every 6 hours, were given for 6 weeks. He became and remained afebrile from the 4th day of treatment. Meanwhile sensitivity tests had shown that the *Streptococcus faecalis*, cultured from his blood on admission, was highly insensitive to streptomycin, the minimum inhibitory concentration being 50,000 μgm. per ml. It was also found that no combination of penicillin, streptomycin, tetracycline, chloramphenicol, erythromycin, novobiocin, vancomycin, or bacitracin completely sterilized the inoculum and that penicillin alone was as effective as anything else.

The patient relapsed soon after leaving hospital. *Str. faecalis*, again cultured from the blood, was still inhibited by penicillin (4 units/ml.) but killed much more slowly; but a combination of 5–10 μgm. per ml. of neomycin and 10 units penicillin was completely bactericidal. Treatment with penicillin 2·5 mega units every 6 hours and intramuscular neomycin 0·5 gm. every 8 hours was therefore given, and continued for 35 days, although the danger of deafness was explained to the patient. He became and remained afebrile after 5 days' treatment. The first signs of deafness were noted on the 28th day; nevertheless in view of the previous relapse the neomycin treatment was continued for 1 week longer. It is admitted that this may have been unnecessary but a further relapse was feared if the course of treatment had been shortened. The patient recovered, but when examined 7 months later he was totally deaf. [There seems a distinct possibility that it might have been better to have stopped the neomycin at the very first sign of loss of hearing, and to have continued for 2 weeks longer with penicillin, perhaps in increased dosage.] *H. Stanley Banks*

WANG, Shih-Heng *et al.* **The Changing Clinical Picture of Scarlet Fever during Recent Years.** *Chinese Med. J.* Peking. 1958, Aug., v. 77, No. 2, 153–61.

This is a review of 2 groups of patients suffering from scarlet fever: the first group of 905 patients were admitted to Peking isolation hospital between 1921 and 1942, the second group of 782 patients between 1955 and 1956. There were striking differences between the 2 groups shown in the following table:

Scarlet Fever

	First group		Second group	
	%		%	
	Incidence	Mortality	Incidence	Mortality
Ordinary	63·8	0·4	97·3	0·1
Septic	31·9	38·4	0·6	20·0
Toxic	3·1	82·1	1·6	16·7
Total		15·0		0·5

The incidence of rheumatic fever was 0·8% for both groups, all except one case developing after the ordinary type. Septic complications occurred in 43·9% in the first group and in 4·0% in the second group. There were 77 cases of acute glomerulonephritis in the first group and 3 in the second group. In the first group 4 systems of treatment were used—symptomatic, antitoxin, sulphonamides and combined sulphonamides and antitoxin: in the second group penicillin was given to all patients. The authors suggest 3 causes for the differences between the groups—the tendency of the disease to become milder, early admission of the patient and the use of penicillin. *A. B. Christie*

TAYLOR, P. J. & MCDONALD, M. A. **Milkborne Streptococcal Sore Throat. A Study of 835 Cases.** *Lancet.* 1959, Feb. 14, 330–33, 3 figs. [11 refs.]

3 epidemics of streptococcal sore throat occurred in the summer of 1957 among young airmen stationed in Cyprus. In all there were 835 patients, of whom 120 had scarlet fever. The common vehicle of infection appeared to be tinned milk diluted with water, and subject to contamination at times after the dilution had been made.

The 3 epidemics each had an abrupt onset, a sudden termination, and a low complication rate; these are characteristics of food-borne, as distinct from air-borne outbreaks of streptococcal infection. There were only 5 cases of acute otitis media (less than 0·6%), 3 (mild) cases of acute nephritis, and no case of rheumatic fever. The men who had had tonsillectomy done in the past appeared to be less susceptible to the disease than those whose tonsils were *in situ* [although no strong statistical evidence for this statement is presented]; but once the illness was established there was practically no difference in the course of the disease as between the 2 groups. *H. Stanley Banks*

GEORGE, J. T. A., MCDONALD, J. C., PAYNE, D. J. H. & SLADE, D. A. **Nephritis in North Yorkshire.** *Brit. Med. J.* 1958, Dec. 6, 1381–2.

In the winter of 1957 and 1958, in York and rural areas of the North Riding, 53 cases of nephritis occurred: in 19 *Streptococcus pyogenes* type 12, or a related type, was isolated: many were either not swabbed or only at an unsuitable time. Attention was first drawn to nephritis in the area when 24 out of 56 boys in a residential school developed pharyngitis followed in 10–19 days by 4 cases of nephritis and 1

of suspected rheumatic fever. Investigations in other schools led to the finding of red cells in the urine of 38 symptomless children, and from 19 of these *Str. pyogenes* type 12 or a related type was isolated.

A. B. Christie

PLEYDELL, M. J. & HALL-TURNER, W. J. A. **An Outbreak of Nephritis in Northamptonshire.** *Brit. Med. J.* 1958, Dec. 6, 1382–3, 2 figs.

This is an account of an outbreak of nephritis in Northamptonshire: there were 89 cases, 73 in children under 16, and invariably the organism found was *Streptococcus pyogenes* type 12. Most of the patients were admitted to hospital and 2 suffered from hypertensive encephalopathy. Long-term penicillin prophylaxis is recommended for the children after recovery and teachers were advised to report respiratory or cutaneous infections occurring in the schools with the aim of possibly excluding temporarily any post-nephritic child.

A. B. Christie

KLEMOLA, E. Antibiotica och immunitet, speciellt vid streptokokksjukdomar. [**Antibiotics and Immunity, especially in Haemolytic Streptococcal Infections**] *Nordisk Med.* 1959, Mar. 19, v. 61, No. 12, 464–8, 6 figs. [14 refs.]

The English summary appended to the paper is as follows:—

"In assessing the value of antibiotic treatment, a negative factor to be considered is that the immunity may be delayed or reduced. Relatively little attention has been paid to this problem. It has been shown in animal experiments that early antibiotic treatment in pneumococcal and tularemia infections can reduce immunity. In man recurrences are common in typhoid and paratyphoid patients treated with chloramphenicol, when the treatment is stopped too early, as it takes time for immunity to develop.

"The most important problem concerns the infections caused by β-haemolytic streptococci. Penicillin treatment delays and weakens the rise in the antistreptolysin titre (AST). However, no definite conclusions can be drawn from the AST changes as regards immunity. The fact that, despite a good primary effect in scarlatina treated with tetracyclines, many bacterial complications caused by the original streptococcus types occur in the weeks following the cessation of treatment, could be due partly to the delayed development of type specific antibacterial immunity. In scarlatina we have good example of a disease in which antibiotics may delay antitoxic immunity, in this case against an erythrogenic toxin of streptococci. Late second attacks more than 3 months after the original disease are no longer uncommon: in Stockholm 4·5% (mean period of observation 2½ years), in Helsinki 5% (mean period of observation 6½ years). The number of cases in which a person acquires scarlatina more than twice is greater than before. In considering the causes of second attacks the moment at which antibiotic treatment is started should be taken into account, as should the time elapsed after the initial disease and the degree of severity of the new infection. Although immunity will be reduced if treatment is started early, it is in general desirable to do so, because the physician concerned cannot take the responsibility for the complications that may arise, all the more as the second attacks are in most cases mild and easy to treat.

"Except in streptococcal infections, the reducing effect of antibiotic therapy on immunity is nowadays probably of no great practical significance. With the discovery of new antibiotics the future situation may be different with regard to both the individual and the community."

HASSALL, J. E. & ROUNTREE, P. M. **Staphylococcal Septicaemia.** *Lancet.* 1959, Jan. 31, 213–17. [19 refs.]

The authors studied the prevalence of staphylococcal septicaemia among patients in the Royal Prince Alfred Hospital, Sydney, during the years 1950–7. From 1950–5 2 to 4 patients were admitted each year with generalized staphylococcal infection; in 1956–7, 16 and 15 patients were admitted. In the years 1952–7, between 2 and 12 contracted staphylococcal septicaemia while in hospital each year, there being an increase over the last 3 years. In 19 of the 46 patients infected outside hospital the origin of the septicaemia was apparently a skin lesion, and in 11 it was in the respiratory tract. In 20 of the 40 patients infected in hospital the origin was apparently from an intravenous infusion (often of long duration) and in 6 it was a surgical wound. 19 (41%) of the patients infected outside hospital died, and 31 (78%) of those infected in hospital.

Staphylococci of phage type 80/81 were responsible for 22 of the 46 extra-hospital infections, and for 13 of the 40 intra-hospital infections. 15 of the 46 extra-hospital infections were with penicillin-sensitive staphylococci, but none of 40 intra-hospital infections.

Clinically the disease had few specific features. Endocarditis was diagnosed in 3 patients who survived and in 9 who died. Meningeal or cerebral involvement was noted in 13. Until the bacteriological results are available, the recommended treatment is with chloramphenicol and erythromycin.

It is considered that the increase in the incidence of the disease arising outside hospital was largely due to the spread of the type 80/81 from hospitals into the general community; the increase in the hospital infections was attributed to the increased prevalence of drug-resistant staphylococci and the increased use of prolonged intravenous therapy. Administration of cortisone, lowering the resistance of some patients, was also a factor.

R. E. O. Williams

JAWETZ, E. **Combined Antibiotic Therapy in Serious Infections caused by Drug-Resistant Staphylococci (1956–1957).** *Arch. Intern. Med.* 1959, Feb., v. 103, No. 2, 289–307, 9 charts. [17 refs.]

Infection with antibiotic-resistant staphylococci is a therapeutic problem requiring much study on the part of the clinician, pharmacologist and bacteriologist.

The present account illustrates the approach of the author to the problem by reference to 11 patients suffering from different varieties of staphylococcal infection. Deep wound infection, staphylococcal endocarditis, pneumonia and empyema, osteomyelitis and septic arthritis are some of the conditions studied. There is some difference of opinion regarding the use of penicillin in very high dosage, *e.g.* 100 million units daily in resistant cases but partial eradication of the organism may be achieved by this means. Rapid emergence of resistance to erythromycin, streptomycin or novobiocin occurs if these are used alone. The author favours combination of antibiotics based on study of the sensitivities in the laboratory. [This is a very detailed study difficult to abstract adequately.]

A. B. Christie

MORGINSON, W. J., WOOD, D. C. & BURGESS, L. **Gamma-Globulin Therapy in Chronic Staphylococcic Dermatoses. A Comparison of Serum Gamma-Globulin Levels and Serum Antibacterial Activity.** *Arch. Dermat.* 1959, Mar., v. 79, No. 3, 305–10. [14 refs.]

"In this study, patients who presented chronic staphylococcic dermatoses were studied: (1) 59% had a reduced γ-globulin level, (2) 70% showed a lowered total serum antibacterial activity, (3) 42% were deficient in the complement-depending (properdin) activity, and (4) 83% demonstrated satisfactory improvement following γ-globulin therapy."

KOZLOVSKAIA, L. A. **The Passage of Measles and Influenza Viruses across the Placenta.** *Problems of Virology.* London. 1958, v. 3, No. 4, 265–6. [11 refs.] [Translated from Russian.]

"The viruses of measles and influenza are able to penetrate to the developing foetus irrespective of the stage of pregnancy and appear in the foetal tissues."

BELL, Julia. **On Rubella in Pregnancy.** *Brit. Med. J.* 1959, Mar. 14, 686–8.

Accounts of 712 cases of rubella during pregnancy have been collected from the literature. With a description of their source, they are set out according to the weeks of pregnancy in which the illness occurred (in groups of 1–4, 5–8, 9–12, 12–16 and over 16 weeks) and by the nature of the defect observed in the child. Such material is highly selected and cannot provide measures of risk; but it may provide at least pointers to those who have to take practical decisions on behalf of individual patients. On this basis it would seem that a history of rubella after the 12th week of pregnancy does not call for abortion while an earlier attack is "such a menace to the normal development of the foetus that it constitutes a risk one cannot allow to be taken for the unborn child".

[Complete dissent from this conclusion followed in the correspondence columns of the *British Medical Journal*. For one attempt to measure the precise risks see this *Bulletin*, 1958, v. 33, 551.]

A. Bradford Hill

ARORA, V. D. **INH and a Combination of Chloramphenicol and Tetracycline in Whooping Cough.** *Indian J. Child Health.* 1959, Feb., v. 8, No. 2, 105–12.

60 children suffering from whooping cough were given 1 of 3 treatments—isoniazid in doses of 10 mgm. per lb. per day for 10 to 15 days, a combination (Ambrasynth) of chloramphenicol and tetracycline in doses of 25 mgm. per lb. per day for 10 days, or a combination of isoniazid with prednisone 0·5 mgm. per lb. per day. 70·7% success is claimed for the first treatment, 57% for the second and 100% (5 patients only) for the third. The author feels that combined isoniazid and prednisone treatment is worthy of further trial.

A. B. Christie

CHATTERJEE, S. K. **Some Social and Epidemiological Aspects of Smallpox in West Bengal including Calcutta—The Problems of its Control and Eradication.** *J. Indian Med. Ass.* 1959, Feb. 1, v. 32, No. 3, 89–103, 2 figs.

Available figures show that in 1957 there were 10,095 deaths from smallpox among 18,612 cases in West Bengal. The figures for Calcutta—which are included —are 3,054 attacks and 2,056 deaths. These figures, though highly inaccurate, provide some indication of the trend of events. In rural areas the responsibility for collecting and transmitting such information lies with the village *chowkidars*. Under this system even death registration has been found to be "defective by 42 per cent". In urban areas where responsibility lies on the relations and medical attendants results have been no better.

In West Bengal over many years a peak in the epidemic cycle of smallpox has occurred every 4–6 years. The 1957–8 crest is considerably lower than its immediate predecessor. In 1957 incidence was higher in the urban than in rural areas; in females than in males; and in age-groups over 10 years as compared with children below that age.

It is obvious enough that what is most needed is an improved system of notification ("intelligence service"), and education (propaganda) to overcome concealment prompted by ignorance, suspicion and superstition etc., and to encourage acceptance of vaccination which under present conditions has often to be carried out by force under police supervision. If a serious attempt were to be made to vaccinate and re-vaccinate the entire population of the State channels of supply of vaccine lymph would need considerable expansion and modification, and such a policy would have to be combined with strict control over the entry of foreigners into the State.

J. Pickford Marsden

i. HARBOE, A. & JUUL, K. Asia-syken belyst ved sykefravaerstall for folkeskole-elevene i en del norske byer. [**The Asian Disease (Influenza) Illuminated by Morbidity Absenteeism from Public Schools in some Norwegian Towns**] *Tidssk. Norske Laegeforen.* 1958, Sept. 15, v. 78, No. 18, 887–90, 3 diagrams, English summary.

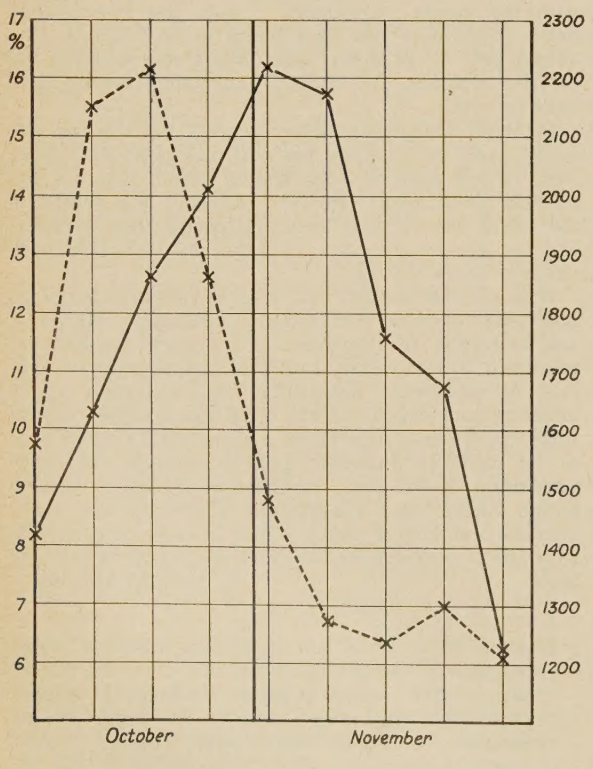
ii. HOVLAND, M. M. Asia-syken blant Skolebarn. **[The Asia Disease (Influenza) among Schoolchildren]** [Correspondence.] *Ibid.*, 1959, March 1, v. 79, No. 5, 291. 1 chart.

On less than one page, the second of the above 2 articles gives a confirmatory answer to the first in which Harboe and Juul say:—

"That the outbreak was limited for some time to one of the town's public schools can hardly be explained otherwise than by assuming that the school's pupils were infected through the school. It seems natural that the same thing happened at the other schools, but it was at this school that this phenomenon stood out with such unusual clarity."

To check up this hypothesis, Hovland has compared the school absenteeism from sickness in Bergen with the sickness rate of adults coming under the national health insurance scheme during the same period in the same town. In the accompanying chart the absenteeism from sickness among the pupils of the public schools in Bergen is recorded week by week during October and November 1957 (the dotted line). The unbroken line refers to payments made during the same period to adults coming under the insurance administration in Bergen. It will be seen that the sickness absenteeism of the pupils rose with explosive force and reached its maximum, 16·2%, in the middle of October 1957. Thereafter it sank quite rapidly and in the second week of November it had come down to 6–7% which is the normal for that time of the year. The curve for the adults rose somewhat more slowly from the beginning of October, and did not reach its maximum till the first week of November. Thereafter there was a rapid fall, and by the end of this month it had reached the normal for that time of the year. As the epidemic was at its maximum among the schoolchildren about 14 days before it attacked adult wage-earners, the conclusion is drawn that during an outbreak of influenza children are infected at school rather than at home. But the closing of schools may yet be stultified if other centres such as cinemas continue to remain open.

Claude Lillingston



HERZBERG, K., MAY, G. & REUSS, K. Untersuchungsergebnisse aus der Influenza-Pandemie 1957/1958. **[Results of Investigations of the 1957/58 Influenza Pandemic]** *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 2, 111–22. [13 refs.]

Between September and the end of December 1957 complement-fixing antibody to the A/Asia strain of influenza virus was found in diagnostic titre in 457 of 1,397 sera from persons resident in Hesse, West Germany, and suspected of suffering from influenza. The main incidence of infection was in October. A second epidemic wave of Asian influenza was observed in the first 3 months of 1958, and during this time a diagnostic titre of antibody was found in 254 of 949 sera. No diagnostic rise of titre could be found in 10 of 11 paired sera examined in haemagglutination-inhibition tests with Asian virus. Asian influenza was accompanied by encephalitis in 36 instances. 18 strains of virus were isolated from 22 patients by amniotic inoculation.

D. J. Bauer

PETERSDORF, R. G., FUSCO, J. J., HARTER, D. H. & ALBRINK, W. S. **Pulmonary Infections complicating Asian Influenza.** *Arch. Intern. Med.* 1959, Feb., v. 103, No. 2, 262–72, 5 figs. [10 refs.]

This is a fairly full discussion of pulmonary infection occurring in association with Asian influenza: 91 patients were treated. Of these, 38 were considered to be suffering from bacterial pneumonia—24 pneumococcal, 6 staphylococcal and 6 from infection due to *Haemophilus influenzae*: 43 had pulmonary infiltrates but no specific pathogenic bacteria were found although 24 of the patients responded rapidly to antibiotics; 10 had acute tracheobronchitis only. In one-half of the patients there was a preceding influenza illness, in the other half the illness began with pulmonary symptoms. 11 patients died, 4 of them elderly but the other 7 were young previously healthy adults: the illness in these patients failed to respond to antibiotics, adrenal cortical hormones and other supportive treatment. Post-mortem examination revealed a haemorrhagic necrotizing pneumonia. Examination of the literature showed that this fulminating post-influenzal pneumonia had been well described in the 1918–19 epidemic.

A. B. Christie

DIGGLE, J. H. **Tracheotomy in Influenza.** *Brit. Med. J.* 1959, Feb. 14, 419–20.

Obstructive tracheitis and laryngitis to a degree requiring operative interference are uncommon in influenza, and few cases requiring tracheotomy have been described. 2 cases, aged 9 and 11 years, in whom the obstruction was severe enough to require tracheotomy and suction are described in this report. In the first there was massive sub-glottic oedema, which caused difficulty in the insertion of an endotracheal tube, and when tracheotomy was done large amounts of frothy blood-stained mucus were sucked out. In the second patient indirect laryngoscopy revealed a grey curtain of hard mucus in the trachea, and a central small hole in this mucus as the only airway. Intubation failed to give relief, and tracheotomy also resulted in no improvement until a hard mucus plug had been sucked out, when further amounts of rubbery blood-stained mucus were more easily removed. Both patients had significant rises of serum titre to Asian influenza A virus, and the mixed bacterial flora in the first patient included *Haemophilus influenzae*, streptococcus and pneumococcus, and in the second case *H. influenzae*, *Staphylococcus aureus* and Friedländer's bacillus, all cultured from the tracheal mucus.

H. Stanley Banks

REEVES, J. T., GARFIELD, J., POLASKY, N. & HAMBURGER, M. **The Treatment of Moderate and Severe Pneumococcal Pneumonia with Oral Phenoxymethyl Penicillin.** *Arch. Intern. Med.* 1959, Feb., v. 103, No. 2, 184–8.

Phenoxymethyl penicillin (penicillin V) was given orally in dosage of 250 mgm. every 6 hours to 110 patients suffering from pneumococcal pneumonia between October 1955 and May 1957. The patients were classified as moderately (61%), severely (34%) or critically (5%) ill. Of the total, 104 showed a satisfactory response, 6 were unsatisfactory. The authors regard oral phenoxymethyl penicillin therapy as effective for pneumococcal pneumonia.

A. B. Christie

BALDRIDGE, G. D. **Immunologic Aspects of Herpes Simplex, Herpes Zoster, and Vaccinia.** *Arch. Dermat.* 1959, Mar., v. 79, No. 3, 299–304, 2 figs. [16 refs.]

After infection with the virus of herpes simplex recurrent attacks of the characteristic eruption can occur in spite of the presence of circulating antibodies "lethal" to the virus itself. Also, no rise in the titre of neutralizing antibody takes place during or after such a recurrent attack. There are 2 practical approaches to the control of recurrent herpes—the avoidance of "trigger" factors, and the use of smallpox re-vaccinations. The success of the latter manoeuvre may be due to suggestion for the viruses of herpes simplex and vaccinia are quite unrelated [and there is evidence that the procedure was founded on a misconception of the term herpes as used in Jennerian times].

Because of the insusceptibility of animals other than man to the virus of herpes zoster little is known of the immunology of this condition, but the rarity of recurrent zoster suggests that immunity of some sort develops during the course of the disease. Results of immunotherapy in zoster with gamma globulin or convalescent serum have been uncontrolled and unconvincing.

Specific immune globulin is available and valuable for the prevention and treatment of cases of eczema vaccinatum and of progressive vaccinia due to dysgammaglobulinaemia. It appears that in many children with agammaglobulinaemia small pox vaccination runs a normal course but that if progressive vaccinia develops in such a patient the outcome is invariably fatal in spite of specific immune therapy.

J. Pickford Marsden

KRUGMAN, S. & WARD, R. **Clinical and Experimental Studies of Infectious Hepatitis.** *Pediatrics.* Springfield, Ill. 1958, Nov., v. 22, No. 5, 1016–22, 7 figs.

A high incidence of infectious hepatitis in Willowbrook State School, Staten Island, led to a trial of gamma globulin in prophylaxis. After a dose of 0·01 ml. per lb. body weight given to approximately one-third of the inmates of 18 buildings, the incidence of hepatitis in the inoculated was 7·4 per 1,000 as compared with 19·7 in the controls over a period of 30 weeks. When the dose was raised to 0·06 ml. per lb. the incidence was 2·5 as compared with 21·4 per 1,000 over a period of 52 weeks. There was therefore evidence of prolonged protective effect, pointing possibly to passive-active immunity. To test this possibility the Willowbrook strain of virus was fed to newly-admitted children shortly after administration of gamma globulin. 0·06 ml. per lb. gamma globulin was given to 11 of 16 children: 30 minutes later all were fed 2 gm. of the virus pool. 4 of the 5 not protected developed hepatitis with jaundice but only 1 of the 11 developed hepatitis, without jaundice. Other investigations showed that virus is excreted in the stool as much as 2 to 3 weeks before the appearance of jaundice.

[See also this *Bulletin*, 1958, v. 33, 641.]

A. B. Christie

WIELOPOLSKA, Anna & WOJCIECHOWSKA, Ludmila. Zachowanie się aldolazy w surowicach ozób z bliskiego otoczenia chorych na nagminne zapalenie wątroby. [**The Behaviour of Aldolase in the Serum of Persons in Close Contact with Persons Suffering from Infective Hepatitis**] *Przegląd Epidemiol.* Warsaw. 1958, v. 12, No. 3, 295–9. English summary (5 lines).

Determinations have been made of the serum aldolase activity in 169 persons who had been in close contact with patients suffering from infective hepatitis. Activities below 30 units were found in 140 (83%), between 30 and 40 in 15 (8·8%) and between 40 and 60 units in 14 persons (8·2%). Repeated examinations carried out at intervals up to 5 months on those persons with an increased aldolase activity showed that the

activity fell rapidly to normal values. The persons concerned showed no signs of illness and were possibly suffering from a subclinical attack of the disease.

D. J. Bauer

COLSON, J. A., GARNUNG, H., HUGONOT, R. & MORAS, P. Le traitement de l'hépatite virale par la métacortandracine. [**Treatment of Virus Hepatitis with Metacortandracine**] *Maroc. Méd.* 1958, July, v. 37, No. 398, 807–9.

The authors have treated 200 patients suffering from viral hepatitis with metacortandracine: a short treatment consisted of 220 mgm. in 10 days and a long treatment 600 mgm. in 20 days. The long treatment appears to have been dropped in favour of the short. The authors are impressed by the effect of this treatment on patients treated in the acute phase. There is a rapid return of well-being, rapid disappearance of jaundice and clearing of the urine. Serum bilirubin and cholesterol rapidly return to normal but the flocculation tests did not appear to be influenced by the drug. There were 2 relapses after treatment but both responded to a second course. In 4 patients who had been jaundiced for more than 3 weeks before treatment with the drug the clinical and biochemical results were not striking. *A. B. Christie*

HEYCOCK, J. B. **Partially Treated Meningitis in Infants.** [Memoranda.] *Brit. Med. J.* 1959, Mar. 7, 629–30.

Pyogenic meningitis is a specially dangerous disease in infancy, partly because early diagnosis is often very difficult in babies. A febrile disturbance, in which the diagnosis cannot be made with certainty in the absence of lumbar puncture, is often treated empirically at home with sulphonamides, given somewhat at random for a few days. The immediate response is favourable, but the dosage of the drug may be inadequate for complete cure. Such partially-treated meningitis in infants is well illustrated by 7 case reports in this article; in 2 cases the causal organism was *Haemophilus influenzae* and in the others probably the meningococcus. The recurrence or continuation of symptoms which brought these babies into hospital some weeks after onset of the disease often took the form of persistent irritability, anorexia, and failure to gain weight—a condition several times diagnosed temporarily as pink disease.

A rather surprising feature in this series is the apparent complete recovery reported in all these patients when energetic antibiotic treatment was given in hospital some weeks after onset. [It should not be concluded, nevertheless, that recovery was in fact complete. Deafness arising in infancy after meningitis may not become apparent for at least 12 months; and who can measure the possible loss in intellectual capacity that may result?] The author suggests that for undiagnosed febrile illness in infants treated in general practice, oral penicillin should be given rather than sulphonamides in order not to mask a possible meningitis that may be present. *H. Stanley Banks*

ROSA, A. & LA PLACA, M. Sulla diffusione degli anticorpi neutralizzanti antipoliomielitici nella popolazione bolognese. [**Distribution of Poliomyelitis Neutralizing Antibodies in the Population of Bologna**] *Riv. Italiana d'Igiene.* 1958, Sept.–Oct., v. 18, Nos. 9/10, 352–72, 3 graphs. [28 refs.]

The English summary appended to the paper is as follows:—

"The results of investigations on the diffusion of neutralizing antipolio antibodies in 559 sera from subjects living in Bologna (age: 0–60 years) are reported.

"It appears that in Bologna natural antipolio immunity is remarkably spread without noticeable differences in the frequency of the three types of antibodies starting from the 5th year of age, the first antibody to appear being the one against type II.

"Comparing the results of these investigations with those got from studies carried out in other parts of Italy, one may observe that the district of Bologna is situated between the South, where natural antipolio immunity is more diffused and earlier acquired, and the North where the percent of grown-ups showing antibodies against all the three types of virus is generally lower."

PAKTORIS, E. A. & VORONTSOVA, L. A. **The Clinical and Epidemiological Characteristics of Poliomyelitis in the Lithuanian S.S.R. in 1956—II.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1788–93, 2 figs. [Translated from Russian.]

This is an account of a severe epidemic of poliomyelitis which occurred in Lithuania in 1955. The majority of the patients were under 3 years but in the country districts about 13% of the cases were over 16 years whereas in Vilnus itself only 2% were of this age-group. The disease appeared to have spread from a children's nursery. There is a strong plea for better diagnosis, stricter quarantine measures and for sending all the cases proven and suspect to one hospital, preferably an infectious diseases hospital.

A. J. Beale

RINDGE, Mila E. **Poliomyelitis in Connecticut—1958.** *Connecticut Health Bull.* 1959, Mar., v. 73, No. 3, 67–70, 1 fig.

During the first 7 years of the 10-year period 1949–58 the annual incidence of poliomyelitis in Connecticut was high. In 1949 there were 654 cases (a case rate of 33 per 100,000 inhabitants) and this number was again recorded in 1955 (case rate 28·8) with never less than 300 cases annually in the intervening years. Poliomyelitis vaccine was first used experimentally in 1954 and has been widely used only since 1956. The value of this vaccination is demonstrated by the figures of incidence of poliomyelitis in 1956 (83 cases, case rate 3·6), 1957 (38 cases, case rate 1·6) and 1958 (42 cases, case rate 1·7).

The experience of these 42 cases in 1958 is described and analysed in this paper. Stool specimens or rectal

swabs from 33 patients were examined and from 21 of these a poliovirus was isolated, 17 of Type I and 4 of Type III. Among these 21 patients only 2 had received a series of 3 vaccine injections. Reference is made to 3 fatal cases and 2 severe cases in patients all of whom were of the 20–29 year age-group and also had received no vaccine. In a comparison of the age distribution of cases in 1953 and 1958 it was found that incidence in the under 5 year age-group was considerably greater in 1958 than in 1953. This fact and also the finding that over one-third of the patients with positive virus isolations were over 20 years of age points to "the need for wider usage of vaccine among pre-school children and among adults."

M. E. Delafield

RUSSELL, W. R. **Management of Poliomyelitis.** *Brit. Med. J.* 1959, Mar. 7, 613–15, 3 figs.

Dr. Ritchie Russell reviews the progress made in the treatment of poliomyelitis since the sudden increase in the epidemic incidence of the disease in Britain in 1947. In countries where life-saving methods have been developed, the death-rate in most outbreaks has now been reduced to about 5% of paralytic cases, from the 20 to 30% of some 25 years ago. [The latter figure is probably an over-estimate; in the Leicester outbreak of 86 paralytic cases in 1926 the case-fatality rate was 12%, and this was similar to that of other outbreaks about that time.]

The management of life-threatening respiratory cases is described in outline. If there is any sign of retention of secretions, the general practitioner should turn the patient into the prone position and raise the foot of the bed; the patient should be transferred to hospital in the semi-prone position, and portable suckers should be available to deal with secretions and vomit. When both throat and respiration are paralysed, tracheotomy with insertion of a cuffed tube is usually required. In the United States many special centres then employ the tank respirator in such cases, and with expert handling good results are obtained. The tendency in Britain is to use the intermittent positive pressure respirator (IPPR), sometimes with minimal negative pressure in the expiratory phase. The IPPR pumps are specially convenient for transporting patients; by this means a safe airway can be provided for a few hours through an endotracheal tube. If poliomyelitis virtually disappears, this work will not be wasted. The same methods can be used in tetanus, infective polyneuritis, myasthenia gravis, and other diseases.

In the case of limb and trunk muscles, splinting and hot packs are more of a nuisance than a real help. The important matter is to change the position of the part through 90 degrees or more every 2 hours, combining this with *gentle* passive movements at most joints. After 2 or 3 weeks as much freedom as possible for voluntary movement should be the aim.

H. Stanley Banks

BATSON, R., CHRISTIE, A., TURNER, Dorothy, MICHAL, Mary & BARRICK, J. H. **The Persistence of Poliomyelitis Antibodies after Primary Immunization of Young Infants.** *Pediatrics.* Springfield, Ill. 1959, Mar., v. 23, No. 3, 550–52.

In a previous report the authors observed a good response of young children to poliovaccine given either alone or combined with pertussis or DPT inoculations. The children were given poliovaccine at 1½, 3 and 10 months of age and 4 months later most had reasonable titres of poliomyelitis neutralizing antibody to all 3 types [this *Bulletin*, 1958, v. 33, 322]. They now report the levels 1 year after the third dose on 55 children. 2 weeks after the third dose 3, 5 and 3 children lacked antibodies to Types 1, 2, 3 and at 4 months the numbers were 9, 4 and 7 respectively. 1 year later there was a marked decline in antibody titre only 4, 23 and 5 children still having titres over 1 : 4 to the 3 types of poliovirus. In view of these results the authors recommend a 4th dose of vaccine 1 year after the third [this *Bulletin*, 1958, v. 33, 932]. They note that so far few untoward effects have been observed with repeated doses of poliovaccine.

A. J. Beale

SVEDMYR, A., VON ZEIPEL, G., HOLMGREN, B. & LINDAHL, J. **Tick-Borne Meningoencephalomyelitis in Sweden.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 8, No. 5, 565–76, 2 figs. [18 refs.]

176 patients with diagnoses of aseptic meningitis, meningoencephalitis, or poliomyelitis from which more than one serum specimen had been obtained were studied. 68 had louping ill neutralizing antibody, or complement-fixing antibody against louping ill or HYPR Czech tick-borne encephalitis viruses in their convalescent sera. Significant increases in antibody titre were demonstrated in 30 patients. In others a significant drop in titre was demonstrated in follow-up serum specimens. Details are given of the antibody pattern in the 68 patients—in many of them until more than a year after onset. For diagnosis the authors recommend the use of complement-fixation tests on paired serum specimens with β-propiolactone-inactivated antigens.

Clinically in 70% of patients the disease had a biphasic course. From a history of tick bite the incubation period was estimated as 2–21 days (mean 7). The first phase of the illness lasted 2–10 days (mean 6) with moderate fever, headache and muscle pains. A symptom-free interval of 2–19 days (mean 8) followed. In the second phase the fever was high and lasted 5–20 days (mean 10) with severe headache, neck rigidity and vomiting. 70% had changes in the electro-encephalogram in the first week, 8 had transient paralyses. The cerebrospinal fluid showed moderate pleocytosis and increased protein.

The cases occurred from June to October with a maximum in August. 70% of the patients gave a history of having been bitten by ticks while on holiday in south-eastern Sweden. In the patients who did not have antibody only 5% had a history of tick bites.

Virus isolation was attempted unsuccessfully from 113 *Ixodes ricinus* from islands north-east of Stockholm. Only 1 of 31 males from the same area had antibody

and none was found in 44 blood-donors from Stockholm. All of 22 cattle sera from the coast north-east of Stockholm had antibody compared with only 1 of 35 from south-western Sweden.

C. E. Gordon Smith

ZAKORKINA, T. N. **Tick-Borne Encephalitis in the North of Omsk Oblast.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1251–3. [Translated from Russian.]

In 1953 in the area there was an outbreak of febrile disease with evidence of meningeal irritation. 3·5% of patients had paretic sequelae. 25% had a biphasic illness and the mortality was 0·7%. Most cases were in a swamp forest area while there was a much lower incidence in an area of secondary birch and aspen forest. Cases occurred mainly in June. 72% were in recent immigrants to the area. 61% were females. Timber workers were particularly affected. All had signs of tick bite. Virus was isolated from the blood of 3 patients 3–5 days after onset and from 2 patients during the 2nd phase 13–15 days after onset. Virus was isolated from 11 of 13 pools of *Ixodes persulcatus* which formed 98% of ticks collected in the area. Virus was also isolated from the brains of bank-voles and northern red-backed voles. The viruses were filtrable and pathogenic for white mice intracerebrally and peripherally. Muskrats were paralysed by intraperitoneal and subcutaneous infection. Guineapigs, rabbits, and adult white rats were insusceptible. Serological tests showed that the viruses closely resembled the Sof'in strain of Russian spring-summer encephalitis virus. Rises in antibody titre were demonstrated in the sera of patients. 23·5% of 102 cattle and horses from the area were found to have complement-fixing antibody.

C. E. Gordon Smith

FEDOROV, I. V. **Reservoirs of Russian Spring-Summer Encephalitis Virus in Wild Birds in the Tomsk Focus.** *Problems of Virology.* London. 1958, v. 3, No. 4, 246–8. [Translated from Russian.]

"(1) The wagtail, common bunting, finch and thrush are virus carriers in the Tomsk spring-summer encephalitis focus.

"(2) The results of examination give grounds for considering birds as reservoirs of Russian spring-summer encephalitis in the Tomsk focus."

LEVKOVICH, E. N. & POGODINA, V. V. **The Alimentary Route of Infection in Tick-Borne Encephalitis.** *Problems of Virology.* London. 1958, v. 3, No. 3, 154–60. [11 refs.] [Translated from Russian.]

This is a study of 102 cases of Russian spring-summer encephalitis believed to have been transmitted in goat's milk. Infections transmitted in milk are becoming increasingly common and account for as much as 48% of cases in some districts. 95 of the cases occurred in groups of 2–8 in families. 25% of the patients were under 5 years of age. Only 3 patients were known to have been bitten by ticks, and the majority were town-dwellers. The incubation period is estimated at 1–14 or more commonly 3–9 days.

Serial serum specimens from the patients were tested for neutralizing antibody and significant rises in titre were demonstrated in most cases. In some cases the response was very late—even after the 8th week. The goats belonging to affected families were found to have neutralizing antibody. 6 strains of virus were isolated: 5 from blood of patients and 1 from goat blood. These strains appeared to be identical with the Sof'in strain.

In search of latent infections due to milk, sera from healthy unvaccinated town-dwellers with no history of encephalitis were tested and about half of them had high antibody levels; their goats were also tested and 13 of 19 found to have antibody. A number of these goats were found to have blood in the milk.

C. E. Gordon Smith

DUMINA, A. L. **Experimental Study of the Extent to which the Tick *Ixodes persulcatus* becomes infected with Russian Spring-Summer Encephalitis Virus as a Result of Sucking the Blood of Immune Animals.** *Problems of Virology.* London. 1958, v. 3, No. 3, 166–70. [Translated from Russian.]

Ixodes persulcatus ticks were fed on animals, with and without Russian spring-summer antibody, which had received virus either by tick bite or inoculation. Ticks only became infected on animals without antibody. The feeding of infected ticks twice on immune animals did not affect the persistence of virus in the tick.

C. E. Gordon Smith

GORCHAKOVSKAIA, N. N., PREOBRAZHENSKAIA, N. K. & DOBRYNINA, L. I. **The Study of the Population of the Tick *Ixodes persulcatus* P. Sch. in the Years following a Single Application of Acaricides to Forest Areas.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1240–50, 3 figs. [20 refs.] [Translated from Russian.]

Studies were made on an island covered with coniferous forest of 2 small areas (6·5 and 8 hectares) which were dusted from the ground with 30 and 50 kgm. of 10% DDT dust per hectare respectively, and of an area of 482 hectares which was similarly dusted with 30 kgm. per hectare. Ticks coming to bite a collector and trapped on a sheet were counted every 5–7 days and control areas were similarly studied. In the control areas 13–17 ticks attacked a man per hour compared with 0·4 tick per man-hour in the smaller areas in the year of treatment; in the 2nd and 3rd seasons after treatment the ticks per man-hour averaged 0·3–3·1% more, but in the 4th season none were found. In the large area no adult ticks could be found by the 3rd season. By infestation studies of red-backed voles (*Clethrionomys*) from the areas larval and nymphal ticks were also shown to have been controlled. Treatment of forest in areas of the order of 10 hectares with DDT as described seems likely to give control

for up to 5 years provided that re-introduction of ticks by animals and birds is not very frequent. Tests of treated forest floor showed that DDT persisted for at least 2 seasons.

Treatment of forest areas with 12% BHC dust from the air was effective only in the year of treatment. This insecticide persisted for a much shorter time than DDT and was not effective in reducing the tick population below a level from which it could not re-establish itself. *C. E. Gordon Smith*

PROC. ROY. SOC. MED. 1959, Mar., v. 52, No. 3, 193–202 (United Serv. Sect. 1–10) [37 refs]. **Symposium on Arthropod-Borne and other Forms of Encephalitis in the Tropics** [HUGHES, W. D.; LEWIS, M. M.; WOOD, P. L. E.; O'BRIEN, W.; INNES, V. M.; HART, R. J. C.].

The symposium began with a general account of the clinical features and differential diagnosis of encephalitis (HUGHES, W. D., *General Clinical Aspects*, p. 193). The following paper (LEWIS, M. M., *General Epidemiology and Prevention*, pp. 193–5) reviewed the zoogeographical background of the arthropod-borne encephalitis viruses and drew attention to their potential military importance when susceptible troops are introduced into an area where an arborvirus is endemic but often almost latent. A review (WOOD, P. L. E., *Japanese B Encephalitis in the Far East*, pp. 195–9) follows of the human epidemiology, clinical features and pathology of Japanese encephalitis. Although there is no specific treatment, much can be done for patients by ensuring that they receive adequate nourishment by intragastric drip and sedation with chlorpromazine where necessary, and by avoidance of complications such as aspiration of food, vomit or secretions. Arrangements for immediate tracheotomy should be available. Frequent changes in posture with percussion of the lung bases may prevent hypostatic pneumonia. The fourth paper (O'BRIEN, W., *African Arthropod-borne Viruses*, pp. 199–201) reviews briefly what is known about arborviruses in Africa where a large number occur. Epidemic encephalitis due to these viruses has not yet been recognized but this might well occur if large numbers of susceptible troops were introduced to a suitable area. The nursing of encephalitis patients is next discussed (INNES, V. M., *Nursing of Encephalitis*, p. 201). The main features are: (1) maintenance of a free airway, (2) adequate fluid and food intake, (3) gentle but effective restraint of violent cases, (4) treatment of hyperpyrexia, (5) control of convulsions, (6) prevention of bed-sores and (7) very careful and frequent observation of patients for changes in their state of consciousness. Air-conditioned mosquito-screened wards are considered necessary for these patients. The last paper (HART, R. J. C., *Laboratory Investigations*, p. 202) discusses the broad approach to virological investigation of endemic or epidemic disease caused by arborviruses. It concludes: "Only when the characteristics and life cycle of the virus are so well understood that preventive measures have achieved perfection is the virologist entitled to consider that his only task is the diagnosis of human disease, and by this time the disease should ideally have been well-nigh eradicated". *C. E. Gordon Smith*

DOWNS, W. G. & ANDERSON, C. R. **Distribution of Immunity to Mayaro Virus Infection in the West Indies.** *West Indian Med. J.* 1958, Sept., v. 7, No. 3, 190–94.

Sera were tested by the haemagglutinin-inhibition and neutralization tests with a locally isolated strain of Mayaro virus. The neutralization tests were done without inactivation of the sera and by intraperitoneal inoculation into 2-day-old mice. Apart from a single positive serum in Antigua, antibodies were found only in Trinidad (8%) and in British Guiana (57%). There was very good correlation between results of the two tests. [The authors state that only 1 serum of 218 was negative by neutralization test and positive by haemagglutinin-inhibition test but, in Table 2, 5 are shown in this category.] About 30% of the population of the Rupununi Savannah region of British Guiana had antibody by the age of 19 years and about 80% over 40 years of age. In Trinidad infections seemed to be mainly localized in the south-east of the island [the map cited is not reproduced]. In this area 50% of the older people had antibody, and males had antibody about twice as commonly as females. This is probably because it is an infection acquired mainly in the forest where the men but not the women usually go to work. *C. E. Gordon Smith*

MATHUR, K. S. & PRASAD, R. **The 1958 Epidemic of Virus Encephalitis.** *J. Indian Med. Ass.* 1959, Jan. 16, v. 32, No. 2, 45–50, 2 figs. [15 refs.]

This is a study of 161 cases of encephalitis admitted to a hospital in Agra from July to September 1958. the peak incidence was between 7 and 21 July. The cases were not localized to any specific part of the town or confined to any social group in the community. 89% of the patients were aged under 8 years and the youngest was aged 1 month. 70% of the patients were male.

The illness usually had a sudden onset often associated with vomiting or the passage of loose offensive stools. High fever was followed by convulsions, mental confusion and often coma. 25 patients had a second febrile episode after 4–10 days' remission. Blindness, impaired vision, and various types of paralysis occurred in a few cases. More than one-half had evidence of meningeal irritation and 42% had extensor plantar responses. Pulmonary involvement was detected in 22%. 35% of the cases were classified as fulminant, 33% as moderate, and 32% as mild. 68% had leucocytosis and the cerebrospinal fluid of nearly 80% had increased cells usually in the range 5–50 per cmm. The sugar was variable and the chlorides and protein normal in the cerebrospinal fluids. The mortality was 28% overall and did not seem to vary much with age. Various regimes of antibiotics, corticotrophin, and a "bland solution containing normal saline—for intramuscular injection" were used in treatment. Patients surviving at least 24 hours after

admission were analysed in their response to the treatments, the treatments being classified as worthwhile or not. There did not seem to be any significant benefit from one treatment rather than another: the response to the "bland solution" was 100% "worthwhile".

C. E. Gordon Smith

Havlík, J. & Potužník, V. Sérologická diagnostika břišního tyfu. Sledování dynamiky titru O a Vi protilátek několika metodami. [**Serological Diagnosis of Enteric Fever. Investigation of the Course of the O and Vi Antibody Titres by Several Methods**] *Časopis Lékařů Českých.* Prague. 1958, Nov. 14, v. 97, No. 46, 1445–8. English summary.

The course of the titres of *Salmonella typhi* complete and incomplete O and Vi haemagglutinins has been studied in 10 patients suffering from typhoid and in 10 carriers. The O haemagglutinin titres were mostly higher than 320 in the patients and increased during the course of the illness, whereas in the carriers the titres were usually lower than 320 and did not show more than a 2-fold fluctuation. Vi haemagglutinins were present in the patients in titres of 4–32 and in the carriers in titres of 32–1,024. *D. J. Bauer*

Cotrufo, P., Colucci, C. F., Finelli, L. & Molese, A. Cortisonici ed associazione CAF-cortisonici nella terapia della febbre tifoide. (Osservazioni su 113 casi.) [**Treatment of Typhoid by Corticoids and Corticoids + Chloramphenicol**] *Acta Med. Italica.* 1958, May, v. 13, No. 5, 113–22. [36 refs.]

113 patients bacteriologically proved (in the majority of cases) to have typhoid fever were treated during 1956 and 1957 in 4 groups as follows:—

Group I. 21 patients were given parenteral cortisone 125–200 mgm. per day for 3 days, then 80–100 mgm. for 7 days according to body weight. 3 patients who did not respond at first received total doses of 1·6, 2·25 and 3·4 gm. respectively.

Group II. 33 patients received prednisone orally or by injection 40–60 mgm. daily for 10 days, 20–40 mgm. for 6 days, 25 mgm. for 2 days. 5 who did not respond or had relapses received total doses of 1·1 gm., the treatment being continued for 25–30 days.

Group III. 29 patients received prednisone orally and prednisolone parenterally 20–30 mgm. daily for 7 days, 15–20 mgm. daily for 3 days and 15 mgm. for 2 days. They also were given at the same time chloramphenicol 1–1·5 gm. daily for 8 days and 1 gm. daily for 6 days.

Group IV (controls). 30 patients were treated with chloramphenicol only, in doses varying from 1 to 1·5 gm. daily for 10 days, then 1 gm. daily for 8 days.

Results: Group I. In 25% defervescence occurred within 48 hours, 2 patients had fever for only 1 day, 4 had relapses, 2 became convalescent carriers, and in 2 either prednisone or chloramphenicol had to be given instead. In 6 both blood and faeces cultures were negative.

Group II. In 15 cases the fever fell by crisis, the shortest period being 8 hours; 11 patients had fever for only 1 day after specific treatment began; 7 patients had 1 or more relapses, 1 died, 2 became convalescent carriers. In 8 patients both blood and faeces cultures were negative.

Group III. In 15 patients fever fell by crisis, the shortest period being 16 hours and in 11 fever lasted for only 1 day after specific treatment began; 1 patient had a relapse, 2 had abscesses, and 1 became a convalescent carrier. In 8 patients both blood and faeces cultures were negative.

Group IV. Fever fell by lysis in all cases and defervescence never took less than 5 days; 2 patients had relapses, one became a convalescent carrier; in 11 cases both blood and faeces cultures were negative. The dosage of chloramphenicol varied from 18 to 30 gm.

The authors point out (1) the absence of haemorrhage or perforation in the patients treated with steroids, the hormone being well tolerated even when given in generous and protracted doses; (2) although steroid hormones by themselves can cure some cases of typhoid if given in sufficient doses for a long enough period, the results are definitely inferior to those obtained with chloramphenicol; (3) the combined steriod + chloramphenicol treatment is far the best; (4) the action of the steroids may be antiphlogistic, antitoxic and antiallergic but the authors are not able to say which is the most important of these.

[In 33 patients both blood and faeces cultures were negative although the O titres were never less than 1 : 320 and some were even 1 : 2,560. No mention is made of any previous TAB inoculations, nor of the ages of the patients.] *W. K. Dunscombe*

Pezzullo, C. & Tedeschi, G. A proposito dell trattamento della tifoide con CAF-fenilbutazone. [**Combined Treatment of Typhoid with Chloramphenicol and Phenylbutazone**] *Acta Med. Italica.* 1958, May, v. 13, No. 5, 129–30. [12 refs.]

The authors have treated with phenylbutazone combined with chloramphenicol 41 patients aged between 7 and 30 years who were both bacteriologically and serologically positive for typhoid. For phenylbutazone the dosage varied according to age and the drug was given in 0·2 gm. tablets, 2 per day for children aged 7–12, 3 per day for persons over 12. 1 tablet was given every 8 or 12 hours for 3 days. 37 patients received 1–2 tablets daily for a further 4–5 days; 3 patients with only slight fever had phenylbutazone only, and 1 had this drug for 4 days when his condition deteriorated and chloramphenicol had to be given as well.

For the 37 patients the dosage of chloramphenicol was one 0·25 gm. capsule every 4 hours till defervescence then every 6 hours for a further 8–10 days. After treatment fever fell by lysis after 36–96 hours with a general improvement in the patient's condition and appetite. A slight reduction in urine output with traces of albumin occurred in children. Symptoms of intolerance were nausea, vomiting, and oedema, the first 2 occurred in about 40% of cases usually on the

4th–5th day. No petechiae, haemorrhage or perforation occurred.

The authors conclude (1) that phenylbutazone + chloramphenicol have a real and constantly favourable effect on typhoid, but they warn against the phenylbutazone because of its action on the blood, (2) that in typhoid the administration of the corticoids + chloramphenicol is preferable.

[No bacteriological details are given; the findings after treatment would have been particularly interesting.] *W. K. Dunscombe*

SEIDLER, L. & ŠVÁB, L. Ein Fall von Paratyphus-B-Bazillenträgertum mit vorwiegender Urinausscheidung bei einem vierjährigen Jungen. [**A Case of Predominantly Urinary Carriage of** *Salmonella paratyphi B* **in a Boy Aged 4 years**] *Ztschr. f. ärztl. Fortbildung.* 1959, Feb. 15, v. 53, No. 4, 260–62. [15 refs.]

In this paper there is a discussion of the features and pathogenesis of the typhoid and paratyphoid carrier states with a report of a case of uncommon type. The case occurred in a boy of 4 years of age who had no history of enteric infection. No evidence of such infection in his family could be obtained. During 1957 he had several attacks of fever of up to 40°C. which lasted for 3 or 4 days. It was then found that these attacks were associated with pyuria which was effectively treated with penicillin. The child was admitted to hospital in early November, 1957 where paratyphoid B organisms were isolated from the urine and also on occasion from the faeces. As the feverish attacks with pyuria continued to occur he was examined by X-ray which revealed pyelonephritis, slight hydronephrosis and dilatation of the ureter on the right side. At operation on March 22, 1958 the right contracted kidney and dilated right ureter were removed. A table sets out the results of the frequent bacteriological examinations of urine and faeces during the child's long stay in hospital. Isolation of paratyphoid organisms was much more frequent from urine than from faeces. The operation has not cured the carrier state as excretion of organisms by urine and faeces has continued, which points to the existence of bacterial foci in other organs of the body.

M. E. Delafield

RUSSU, V., NAS, Ligia, SUCIU, T., DORIN, P. & ULMEANU, C. Studiul eficienței vaccinării orale si mixte T.A.B., prin testul epidemiologic. [**A Study of the Efficiency of Oral and Combined T.A.B. Vaccination by means of the Epidemiological Test**] *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, May–June, v. 3, No. 3, 257–68. [19 refs.]

An investigation has been made of the efficacy of an oral typhoid vaccine in comparison with TAB vaccine. The oral vaccine contained *Salmonella typhi, Salm. paratyphi A* and *Salm. paratyphi B* in the ratio of 4 : 1 : 1 in a concentration of 10^{10} organisms per cc.; 3 doses of 10 cc. with the addition of 20% of alcohol were given at intervals of 1–2 days. Vaccination was carried out on persons living in an area where the incidence of typhoid was low; some persons also received a single dose of TAB vaccine 25 days after the oral vaccine, and others received TAB vaccine alone [the numbers treated are not stated]. No local reaction was observed after oral vaccination, and a general reaction occurred in only 7·5% of persons, compared with 71·7% of those given TAB vaccine. In the 2 years after vaccination (1954–5) the incidence of typhoid in vaccinated persons was lower than in a comparable group of vaccinated persons, and favourable results were obtained with the oral vaccine [the incidences in the different groups are given in detailed tables, but the conclusions cannot be presented concisely as the results are not summarized].

D. J. Bauer

NAUMANN, P. & RÖHRS, H. Ein Beitrag zur Frage der *Salmonella*-Doppelinfektion. [**Double Infection with Salmonellae**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 2, 103–10. [Numerous refs.]

This is the history of a 59-year-old male patient admitted to hospital with advanced Hodgkin's disease. On admission he complained of urinary symptoms and was found to have a severe cystitis. *Salmonella typhi-murium* was repeatedly isolated from his urine on culture. Routine examination of the patient's stools now yielded Salm. Blockley on culture. During the month before he died of his primary complaint, intensive examination of stools and urine, sometimes with investigation of up to 50 single colony picks from primary cultures on appropriate media, consistently failed to demonstrate a mixture of the 2 salmonella types in either stool or urine. At post-mortem, cultures confirmed the independent distribution of the 2 pathogens in the patient's tissues. *Salm. typhi-murium* alone was isolated from cultures of spleen and both kidneys, and Salm. Blockley from the liver, gall-bladder, stomach, duodenum, jejunum, caecum and rectum.

B. Moore

DRACHMAN, R. H., PETERSEN, N. J., BORING, J. R. & PAYNE, F. J. **Widespread Salmonella Reading Infection of Undetermined Origin.** *Pub. Health Rep.* Wash. 1958, Oct., v. 73, No. 10, 885–94, 1 chart. [23 refs.]

During the 12 months from September 1956 to September 1957 there were 325 acute sporadic infections and 3 outbreaks of Salmonella Reading infection throughout the U.S.A. The maximum incidence was in February 1957. Infants and children were mainly affected, 18% of the patients were under 1 year old and 11% were under 6 months.

This outbreak contrasts markedly with the previous extremely low incidence of Salm. Reading infections—only 24 cultures were received by the Communicable Disease Centre in the 8 years up to 1956.

Although no definite explanation could be found for this widely scattered outbreak it was noted that it began around the time when there were a small number of outbreaks of Salm. Reading infections in poultry, and infected poultry might have been distributed so as to cause the human infections. *J. Nagington*

VAL'VACHEV, N. I. & ROMANOV, B. G. **An Institutional Outbreak of Boyd-Novgorodskaia III Dysentery.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 5/6, 673–8. [11 refs.] [Translated from Russian.]

An explosive outbreak of dysentery is described which occurred in a community of 258 people in one building. From 14 people who had a mild attack of dysentery and 59 others who were symptomless *Shigella boydii* type 3 was cultured. None of those affected excreted the organism for long—only 9 excreted it for 10 days and the longest carriage was 27 days in one person. It is considered that chronic carriers probably play little or no part in the spread of this infection.

[Boyd-Novgorodskaia III is the name given in Russia in 1952 to the organism first described by BOYD in 1932 as P274 and first identified in Russia by NOVGORODSKAIA *et al.* in 1943.] *J. Nagington*

CHU, Shou-Ho. [Compiled by.] **Artificial Hibernation in Treatment of Toxic Dysentery.** *Chinese Med. J.* Peking. 1959, Feb., v. 78, No. 2, 120–25.

Toxic dysentery is a type of acute bacillary dysentery characterized at the onset of the disease by high fever, convulsions and coma along with disturbance of the circulatory and respiratory centres. These symptoms usually precede any obvious gastro-intestinal symptoms. Figures from 7 Peking hospitals in 1957 showed a mortality of 22·8%. In the present series 95 children were treated with artificial hibernation and there were only 4 deaths, all due to respiratory failure. Hibernation was induced by the intravenous or intramuscular administration of chlorpromazine 50 mgm., phenergan 50 mgm. and dolantin 100 mgm. When the child fell asleep, ice bags were used. Temperature was usually maintained at 35°–36°C. Chloramphenicol was given by intravenous drip or nasal tube and fluids were given intravenously as required. The purpose of the hibernation was to put the nervous system under a state of protective inhibition against sudden exogenous stimuli, to reduce metabolism, diminish oxygen consumption and enable the patient to recover from the state of shock so that the antibiotic could then have a chance of dealing with the infection. From the figures quoted, it would appear that the treatment was successful. *A. B. Christie*

TUBERCULOSIS

MURATOVSKI, G. Kretanje smrtnosti od tuberkuloze kod dece u NRM od 1947 do 1954 god. [**Tuberculosis Mortality in Children in Macedonia between 1947 and 1954**] *Tuberkuloza.* Belgrade. 1957, Sept.–Dec., v. 9, Nos. 5/6, 354–60, 6 graphs. German summary.

The annual mortality from tuberculosis in Skoplje, Macedonia, between 1945 and 1954 was 18·9 per 10,000, compared with 16·5 in 8 other towns in the same province. The tuberculosis morbidity in the province, with a population of 1,300,000, was estimated at 2·1%. 24·4% of fatal cases occurred in children up to 15 years of age, and 42·5% in persons aged 16–40 years.

D. J. Bauer

MOLLER, A. V. **Mass Radiography in Denmark.** *Nordisk Med.* 1958, Aug. 21, v. 60, No. 34, 1189.

This is an introductory note without detailed findings.

PÄTIÄLÄ, J. **Mass Radiography in Finland.** *Nordisk Med.* 1958, Aug. 21, v. 60, No. 34, 1190–91.

A few main findings are quoted.

WEGELIUS, C. & WIJKSTRÖM, S. **Mass Radiography in Sweden.** *Nordisk Med.* 1958, Aug. 21, v. 60, No. 34, 1191–4. [17 refs.]

This contains a table which sums up the work done and the findings made in the various countries and towns since 1943; it includes non-tuberculous conditions.

KÄLLQVIST, I. **Long-term Prognosis in Pulmonary Tuberculosis detected by Mass Radiography. A County-Wide Survey with Controls and a Comparison between Two Mass Surveys with a Seven-Year Interval.** *Acta Tuberculosea Scandinavica.* 1958, Suppl. 44, pp. x + 177, 31 figs. [Numerous refs.]

The value of mass X-ray surveys as a method of discovering unsuspected cases of pulmonary tuberculosis is undoubted, although it has been shown that surveys of specially selected groups is often more productive; but comparison of fate of those patients detected by the mass surveys and those detected on clinical grounds is more difficult. This article starts with a survey of similar articles which have dealt with the subject. The author finds that none of them are wholly satisfactory, mainly owing to the difficulties of following up a sufficiently high proportion of patients.

The circumstances in Sweden, especially accurate notification and hospital discharge reports, made this less difficult. The papers report on 172,459 patients over the age of 7 years who underwent a mass X-ray survey in Sodermanland in the period October 1946 to January 1949. This represents 96·7% of those invited to attend. 5,667 were picked out as requiring further investigation. Of these 676 persons were notified and regarded as having unhealed tuberculosis, and 275 were placed under supervision as having lesions which although apparently inactive had possibilities of breakdown. For prognostic comparison 292 consecutive patients who had had pulmonary tuberculosis diagnosed on clinical grounds were selected.

The follow-up period was from 8 to 10 years, or until death or cure; and in order to give various factors due significance the homogenization method for statistical analysis was used.

Initially the patients were classified as regards the extent of the disease by the National Tuberculosis Association (NTA) of America classification modified to show excavation and bilateral distribution. They were then assessed as initially active, inactive, probably active, probably inactive, and initially not active, later active.

Far advanced disease was found in 41% of the survey, and 17% of the control group. A total of 339 cases in the survey initially active compared with 248 in the control series.

In the control group 21% died of pulmonary tuberculosis during the first year, against 4% in the survey group in the first year after diagnosis, and at the end of 8 years 29% of the controls and 12% of the survey cases had died. After the same period 63% of survey and 50% of the control cases were medically satisfactory. Satisfactory economic results were found in 78% of the survey and 60% only of the control group.

Of the cases in whom retrospective review failed to find definite tuberculous activity, those classified as inactive constituted 21% of the survey and 5% of the control groups. Of the groups probably active and probably inactive, 22% of survey and 9% of the control group, one-third died of other causes than tuberculosis before the stipulated period had elapsed, explained by the high percentage of older age-groups.

The group initially non-active but later active is interesting; it comprised 7% of the survey as against 1·5 of the control group. In combination the risk that the disease would become active in patients classified as having inactive or probably inactive disease was 8% after 8 years against 4% after 5 years.

The mortality in patients with mental illness or deficiency was higher than normal, but this could largely be ascribed to the high proportion of advanced cases. 275 patients were considered to have disease so soundly healed as to render notification unnecessary, but retrospective survey showed that 12 had in fact active disease at the time, and 21 non-active initially developed active disease later.

A second mass X-ray survey was done between 1953 and 1955. 1·1 per 1,000 persons examined were considered to need notification in this survey, compared with 1·9 per 1,000 in the first survey. Only 8·3% of the subjects in the second survey had advanced disease compared with 17·1% in the first survey.

The influence of better treatment is shown by comparing the mortality of the active cases in the two surveys at the end of 3 to 4 years with that after the same interval in the first survey. Of the 130 patients available for analysis in the second survey 1·5% died, compared with a mortality of 10·7% in the first survey.

The author concludes that the earlier diagnosis produced by the mass survey leads to a substantial improvement of prognosis of cases found by this method compared with those found as a result of routine methods. This is an elaborate and very carefully controlled investigation which gives an emphatic answer to the questions the author set out to elucidate. Probably only those specially interested will find time to master all the statistical tables which are a feature of the paper, but a 10-page summary will enable a reader to understand the conclusions. *F. H. Young*

AWAN, A. H. & DAR, M. S. **T.B. Survey of Mozang High School, Lahore.** *Pakistan J. of Health.* 1958, Apr., v. 8, No. 1, 19–20.

Because of inadequate tuberculosis morbidity and mortality returns in Pakistan surveys of small groups are being carried out in order to obtain data on which to assess the extent of the tuberculosis problem. One such survey which disclosed an incidence of active pulmonary tuberculosis of 6·9% in factory workers in Lahore has already been noticed in this *Bulletin* [1956, v. 31, 616].

In the early part of 1958 a survey was made in a high school in Lahore. The pupils belonged mostly to the poor and middle classes and were aged 10–20 years. The tuberculin reactor rate in 957 who were tested was 67·77%. 759 pupils were fluoroscoped, of whom 34 showed appearances suggestive of tuberculosis; these were X-rayed and pulmonary tuberculosis was diagnosed on radiological grounds in 26 (3·47%). Tubercle bacilli were found in direct examination of the sputum in 10.

Details are:

Age group	Enrolled	Fluoroscoped	X-rayed	Pulmonary Tuberculosis	Incidence
10–14		640	29	22	3·44%
15–19		107	5	4	3·74%
20 and over		2	0	0	0
Total	995	749	34	26	3·47%

[It is not clear whether the above figures refer to primary or post-primary pulmonary tuberculosis or to both. In any case they demonstrate the epidemic nature of pulmonary tuberculosis in Lahore and the extent of the problem facing the public health authorities.] *H. G. Calwell*

WARMINGTON, W. T. **Tuberculin Sensitivity in Co. Fermanagh, N. Ireland, 1952 55.** *Ulster Med. J.* 1958, Nov. 1, v. 27, No. 2, 158–61. [10 refs.]

County Fermanagh is a predominantly rural area of Northern Ireland with a population of some 52,000. It was previously found by Warmington (*Ulster Med. J.*, 1955, v. 24, 143) to have a low tuberculin reactor rate and he has carried out tuberculin surveys on similar groups to those examined in 1949–51 in order to see if the falling incidence of tuberculosis is accompanied by a falling reactor rate.

The first group studied comprised 965 persons attending the Chest Clinic. No material reduction in the reactor rate was found under the age of 15, which finding Warmington attributes to the high proportion of contacts among the children. In the group aged 15–35 the rate fell from 53·4% of 502 persons to 28·2% of 389 and in those over 35 years from 62·8% of 183 persons to 46·7% of 75 persons. The fall in the 15–35 group is regarded as statistically significant. The test used in this chest clinic group was the Mantoux with 1 TU because that test had been used in 1949–51.

In the second group which comprised public schoolboys the reactor rate was 18% of 88 boys compared

with 29% of 169 boys earlier. This fall was regarded as "just statistically significant".

The third group was of factory workers and the Heaf test was used but Warmington "corrected" the results on the basis that the Heaf test gives only 86% accuracy compared with the Mantoux test with 100 TU of OT. He does this because IRVINE [this *Bulletin*, 1955, v. 30, 294] "using O.T. on 243 persons found 86 per cent. accuracy for the Heaf test". He mentions, however, that CALWELL in a trial on 1,335 children found 99·5% agreement between the 2 tests (*Brit. Med. J.*, 1954, v. 2, 1292).

The results were:

	Total Tested	Positive	Reactor Rate	
1949–51	431	223	51·7%	(Mantoux 100 TU)
1952–55	328	107	32·6%	(Heaf test)

The rates in females were 36 and 27·4% respectively and in males 62·5 and 40·5% respectively. The rate in females was already low at the date of the first survey and remains well below the male rate.

Warmington advocates BCG vaccination for the many young non-reactors who emigrate from Fermanagh. *H. G. Calwell*

SALLINEN, P. **The Finnish Intradermic Tuberculin Test.** *Acta Tuberculosea Scandinavica.* 1959, v. 36, No. 4, 265–76, 2 figs. [21 refs.]

The Trambusti tuberculin test as originally described was performed by dipping an injection needle into a 1 : 9 solution of Old Tuberculin and inserting the point into the skin. In the Finnish modification of the test a drop of undiluted tuberculin (OT or PPD) is placed on the skin and the needle point is inserted into the skin through the tuberculin. This modified method and the original were both used in the investigations described by Sallinen.

Both methods of application used at the same time in natural reactors resulted in induration in the same persons, and there was no statistically significant difference in the average size of induration. It was found best to read tests after 72 hours; the criterion of a positive reaction is 5 mm.

The modified test (described as FT) was used in a comparative trial with the Mantoux test to detect tuberculin sensitivity in schoolchildren vaccinated with BCG 4–5 months previously. The FT test was considered to have the advantage of causing less intense reactions than the Mantoux test and at the same time to give a positive reaction in every case where the Mantoux test was positive. The most suitable site for the test was found to be the radial margin of the volar aspect of the upper forearm.

At mass examinations the single Finnish test was as reliable as the 2-stage Mantoux 5–100 TU test both in rural and industrial communities and in vaccinated and unvaccinated persons. One-half of the subjects aged over 40 years who were negative to the Finnish test were found to react when the needle was inserted at the same site a second time. In the younger age group it was exceptional to find a reactor only to the double test.

The incidence of complications was studied in 2 areas. Vesiculation was most frequent (11%) in unvaccinated men aged 30–50 years, and lymphangitis was most frequent (2%) in unvaccinated males aged 15–30 years. These complications were relatively rare in vaccinated persons.

The size of induration was studied in vaccinated and unvaccinated persons. The frequency of strong reactions was greater in the older vaccinated group—a sign of reinfection. It was also greater in vaccinated males than in vaccinated females.

The method of tuberculin testing described above was developed in Finland because of shortage of nursing and medical staff. It has now been used for over 10 years and over 4 million tests have been done.

H. G. Calwell

CORY, R. A. S. **A Tuberculin Survey in the Island of Montserrat, British West Indies.** *Brit. J. Dis. Chest.* 1959, Jan., v. 53, No. 1, 99–108, 2 figs.

This survey was made under the auspices of the World Health Organization in 10 days towards the end of 1957. Its object was to determine the needs of the island of Montserrat for a mass BCG vaccination campaign.

Montserrat (population about 14,000) is in the British West Indies. The main occupations are agricultural and many of the people work their own farms. The capital town has a population of some 4,000. There is little travel between the island and the other West Indian islands and the chance of the importation of tuberculosis is at present negligible. However, during the past few years emigration of adults to England has become common and there is a possibility that some of them may contract tuberculous infection there and return home to spread it. The homeward drift has not yet started.

No X-ray facilities are available, and the extent of tuberculosis has to be assessed by tuberculin survey. In 1957 there were 5 deaths from tuberculosis (35/100,000) and in December 1957 there were 26 known cases of the disease.

In the course of the present survey 2,924 persons received a single Mantoux test (5 TU of PPD), of whom 192 (6·5%) failed to return for reading.

The reactions of all individuals were:

Reaction	Total	Percentage
Negative	1,880	69
Doubtful	310	11
Positive	542	20

In the group of 303 adults who completed the test the reaction was positive in 61%. A very strong reaction suggesting the presence of active or potentially active tuberculosis occurred in 12%.

In the group of 64 school teachers who completed the test 42% were reactors, none of whom showed reactions of over 15 mm. in diameter.

In the group of 93 children not attending school, who completed the test, 15% were reactors of whom 3 had strong reactions.

As the schools in the island were too numerous to cover in the time available 11 were chosen for survey in 2 areas where most of the known persons with tuberculosis lived. The number of children who completed the test was 2,272 of whom 14% reacted. There were 45 with strong reactions including 21 under 9 years of age.

There were differences in the reactions shown by urban and rural children as follows:

Age-Group	Reactor Rate % Urban	Rural	Totals on which based
0–4 years	0	0	12
5–9	13	5	1,214
10–14	33	12	1,010
15–16	30	37	36

The discrepant result in the oldest age-group is attributed to the finding that in one school 4 out of the 5 pupils in this group were found to be reactors.

It was thus shown that tuberculous infection in adults in Montserrat is widespread; the rate is low in young children but rises with age. Rural schools in areas where known cases have occurred show a higher infection rate than those in "clean" areas.

H. G. Calwell

BREATHNACH, C. S. **The Source of Infection in Primary Tuberculosis.** *Med. Officer.* 1959, Mar. 6, v. 101, No. 10, 133–4.

In 1957 an attempt was made to follow up the 465 children who attended the Primary Tuberculosis Centre, Dublin (population 539,476), with primary infection for the first time in 1951. Bovine infection was regarded as having been of little importance in the series.

The number of children followed up was 281. The infection was traced to an active case of tuberculosis in 262 children of whom 156 were reviewed in 1957 (*i.e.* reviewed plus deaths). Details are given thus:

Age (years)		Mother	Father	Other Family Contact	Frequent Other Contact	Infrequent Other Contact	None Known	Total
0–1	1951	15	21	0	7	0	12	55
	(1957)	(9)	(15)	(0)	(5)	(0)	(9)	(38)
2–5	1951	42	48	7	22	6	84	209
	(1957)	(27)	(36)	(5)	(11)	(5)	(55)	(139)
6–11	1951	14	35	15	11	3	84	162
	(1957)	(5)	(15)	(8)	(9)	(2)	(52)	(91)
12–14	1951	6	8	2	0	0	23	39
	(1957)	(0)	(4)	(0)	(0)	(0)	(9)	(13)
Total	1951	77	112	24	40	9	203	465
	(1957)	(41)	(70)	(13)	(25)	(7)	(125)	(281)

It was thus seen, that the source of infection was found more often in younger than in older children. In the older child there was less likelihood of finding the source so that in only 1 child in 5 under 2 years of age was there failure whereas the source was not found for almost 2 out of every 3 children aged 12–14 years.

Contact with an open case was discovered in 262 children (56·3%). In 77 (16·6%) the mother and in 112 (24·0%) the father was the infector, while in 73 (15·5%) the source was some other relative or, almost twice as often, extrafamilial.

60 mothers infected 77 children (1·3 per mother) and 79 fathers infected 112 children (1·4 per father). The finding that the father was more frequently the source of infection than the mother was attributed to the greater tuberculosis morbidity in males from about the twentieth year onwards.

H. G. Calwell

MYERS, J. A. **The Natural History of Tuberculosis in the Human Body. I. The Demonstrable Primary Pulmonary Infiltrate.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 19–30, 3 figs. [16 refs.]

This is a very long-term study of the course of primary pulmonary tuberculosis. After a review of the literature Myers considers the history of the 19,045 children who attended the Minneapolis clinic between 1921 and 1941.

300 children were observed with primary infiltrations demonstrable by X-rays. These vary from shadows hardly demonstrable to dense homogeneous areas which could appear in any parts of the lungs. When they were present in positive tuberculin reactors at the first examination it was only by observation that they could be differentiated from other disease conditions or the reinfection type of tuberculous lesions.

In the group of 300 children symptoms were usually absent or minimal. In 1935 the author reported that the clinical course was benign in the 136 patients available for review, and that this occurred whether the children were treated at sanatorium, a special school, or at home.

267 were traced in 1958 (10 of these could not be re-examined); 26 had died.

Of the 26 patients who died, 9 died of tuberculosis, 7 of acute disease and 2 of chronic pulmonary tuberculosis at the age of 12 years and 22 years of age respectively.

Of the 241 present survivors complete information was available for 231. Of these 9 developed clinical tuberculosis, and 222 remained free of clinical disease, but as they are on an average only just over 30 years of age, there is plenty of time for clinical tuberculosis to appear, so no final conclusion can be drawn. The possibility that similar investigations can be done has gone, as now only 4% of grade school children have a positive tuberculin reaction, and antimicrobial drugs are often administered when a positive skin test is discovered. This group of 300 children is not comparable with those reported from sanatoria and hospitals.

The author thinks that the reason why most of the primary lesions are benign is that their development begins in non-sensitized tissues. In fact demonstrable primary infiltrates behave so differently from the reinfection type of lesions that they might be caused

by a different aetiological agent. This makes it very important that the two should be distinguished. The fact that the primary lesions are so benign does not diminish the importance of protecting children against infection. *F. H. Young*

KAIDA, K. *et al.* **Studies on the Apical Localization of Pulmonary Tuberculosis.** *Kyushu J. Med. Sci.* Fukuoka. 1958, June, v. 9, Nos. 2/3, 110–26, 13 figs. [15 refs.]

The problem of the apical localization in pulmonary tuberculosis has been discussed for many decades, but a completely satisfactory explanation has not been produced. The authors of this paper divide the problem into two. Are the apices a place of *locus minoris resistentiae* (LMR), and if so why? or have the tubercle bacilli a special tendency to infect the apices, and if so what is the route of the infection? A combination of the two thus gives rise to 4 possibilities.

To clarify the problem of LMR the authors, by inserting a Metra catheter into the various bronchi, showed that in normal respiration the pressures in the lower lobes were lower than in the upper, but the amount of air flowing into each was similar. By gas analysis it was claimed that in the erect posture the percentage of O_2 in the alveolar air was 2·08% higher than in supine, but the opposite result occurred in the lower lobes. By using right heart catheterization they found that in the supine position the blood flow and oxygenation were reduced in the upper lobes compared with the lower—in the right lung the figures obtained for blood flow were 0·25 litre per min. in the upper lobes, and in the lower 2·85 litres per min. The oxygen saturation of the blood was reduced in the upper lobe vessels and was also further reduced in standing position. FISHBERG (*Pulmonary Tuberculosis.* 1922. Philadelphia: Lea Febiger) is quoted as saying that there is stagnation of the lymphatic flow in the apico-dorsal part of the upper lobes and the upper part of the lower lobes.

The authors found that in 54 cases in which they have been able to find out the route of infection of the apices 66·6% arose by bronchogenic spread from the primary focus. Turning to the probability of lympho-haematogenous spreading, it was thought that calcified lymphatic glands gave rise to secondary lesions after a long period of lack of radiological symptoms. In 1,613 patients those with lesions in the lungs had calcified glands in 24·98%, whereas in those without lesions in the lungs only 13·50% had calcified glands.

By experiments on rabbits the contention of MEDLAR and SASANO that a *locus minoris resistentiae* was produced in the apices of the lungs by keeping rabbits in the upright position was confirmed. Injection of infective material into rabbits' ear veins was more likely to produce apical lesions than if the injection was made into the femoral vein.

[A vast amount of work is summarized in this article but the necessary lack of detail makes the critical assessment difficult. Some of the argument is a little hard to follow, but the article is worth reading by those interested in the subject.] *F. H. Young*

EDGE, J. R. & BOTTRILL, D. E. **Resection for Pulmonary Tuberculosis.** *Brit. Med. J.* 1959, Jan. 31, 276–8.

This paper deals with 170 patients who had resection for pulmonary tuberculosis. They were divided into 2 groups. Group I consisted of 95 patients who had received for a minimum of 6 months continuously at least 2 of the standard drugs daily, in doses of streptomycin 1 gm. with isoniazid 200 mgm.; isoniazid 200 mgm. with PAS 10 gm.; streptomycin 1 gm. with PAS 15 to 20 gm. Group II consisted of 75 patients who had had antibiotic treatment inadequate by the above standards.

The proportion of large cavities and more widespread areas of disease was higher in group II; but the authors do not consider the results were due to this because none of the 13 patients in group I who had cavities larger than 5 cm. produced culture-positive specimens, whereas 17 out of 26 of similar cases in group II had culture-positive specimens.

15% of specimens were culture-positive in group I compared with 52% in group II. The incidence of patients whose specimens were smear- and culture-negative was twice as high in group I as in group II. 52% of group I, and 33% of group II, were smear-positive and culture-negative [? dead organisms].

In group I, of 14 culture-positive specimens 4 were fully sensitive, 3 resistant to all drugs, and 7 resistant to one drug. In 1 of the fully resistant group and 3 of the partially resistant group no positive sputa had ever been obtained.

In group II positive-culture specimens were obtained from 39 patients; 5 were sensitive to all, 6 were resistant to 1, 13 resistant to 2, and 15 resistant to all drugs.

Where pre-operative positive sputum was available, the resistance corresponded to that of the specimen bacilli.

At the end of 15 months to 4 years after operation, 94 patients in group I were well, and 1 had died of acute dilatation of the stomach the day after operation. In group II 62 (83%) were well, 6 still had active disease, and 7 had died (4 of tuberculous complications and 3 from non-tuberculous causes).

On the bacteriology findings alone the authors conclude that out of the 95 group I patients, operation was unnecessary in 31, doubtfully necessary (smear-positive, culture-negative) in 50. Of the 14 culture-positive patients 4 had had fully sensitive bacilli, and would probably have responded to further drug treatment, 7 showed partial resistance, and might have responded to a 3-drug regime, and 3 were fully resistant which called for surgery. Because pre-operative cultures were negative bacterial resistance was not discovered until the specimens were cultured. Similar findings occurred in group II.

The results described were excellent in group I, and the authors wonder if surgery was necessary in 85 of the 95 patients. [In all probability this conclusion is correct, but must await confirmation that the smear-positive uncultivable bacilli are innocuous. Apart from this some surgeons like to resect areas of lung which show any evidence of tuberculous histology. This is

an excellent paper, full of meat in a short space, and shows conclusively the need for full pre-resection therapy.] *F. H. Young*

LARGE, S. E., LAIRD, A. N. & HARRISON, G. K. **Lung Resection for Tuberculosis in the Army. A Report on 61 Cases.** *J. Roy. Army Med. Corps.* 1958, Oct., v. 104, No. 4, 216–22.

This article deals with 64 resections performed on 61 service personnel suffering from pulmonary tuberculosis. Adequate drug treatment was given before operation. Resections were undertaken on 9 lungs with solid lesions, more or less unchanged by chemotherapy, 45 patients who had had cavitation but whose cavities had closed on chemotherapy, and 10 where cavitation persisted. The mortality was nil, and the complications (10) were not serious. 1 bronchopleural fistula, 1 empyema, 1 pulmonary embolus, and 1 localized wound infection were the most important. At first chemotherapy was continued for 3 but later for 12 months after operation. No relapse has been noted. 59 patients were returned to duty, at first in category P7 (the Pulheems system of classification) and gradually upgraded to P3. It is thought that some patients will be upgraded to P2 5 years after operation.

The need for extra certainty that relapse will not take place in service personnel is paramount, so some patients were operated on who might have been merely put under observation in civilian life.

Although satisfied with the results, the authors feel that as a result of further reports on the stability of some lesions after prolonged chemotherapy they may in the future decide that the operation will be unnecessary in some cases similar to those in which resection was performed in this series. *F. H. Young*

PECORA, D. V. **The Importance of Preresection Drug Therapy for Pulmonary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 41–6, 4 figs.

Although it is agreed that pre-resection antimicrobial therapy is advisable, the length of time it should be used before operation is not decided, especially as some authorities think that there is a danger that drug resistance will develop. The author has reviewed 328 resection cases from the point of view of the length of persistence of positive cultures from both sputum and resected specimens. Graphs are given to illustrate various results. Throughout the study patients in whose sputum resistant organisms appeared were eliminated.

The effects of various drug regimens on the yield of culturable bacilli in the sputum is considered as a start. Single drug therapy results fell far short of those obtained when multiple drug therapy was used, especially if isoniazid was a constituent. By the end of 6 months, the triple drug, and streptomycin and isoniazid groups all failed to grow bacilli. After 6 months' therapy the additional percentage converted under the other combinations only increased very slowly.

Where the cultures were made from resected specimens, the percentage of cases in which bacilli were demonstrated microscopically did not vary much with the various therapeutic regimens, and especially when therapy was carried out for longer periods. There were about 10% more positive results from the resected specimens than from the sputum. It was not possible to correlate the bacteriology with the pre-treatment extent of disease. On the multiple drug regime the percentage of patients in whom bacilli could be cultured from the resected specimens was during the first 6 months much greater in cavitated lesions, but after 10 months' therapy no bacilli could be grown from any of the 25 cavitated lesions.

When the emergence of resistant organisms in the 224 resections was reviewed, they were found in 1 of 82 patients (1·2%) who received various combinations including isoniazid, and 7 of 142 patients (5%) who received streptomycin and PAS. 5 of 63 patients (7·9%) who had cavitated disease, compared with 3 of 161 (1·9%) who had non-cavitated disease, developed resistant organisms.

Since 1950 no complication has occurred during the month following resection, and only 2% of late complications in those patients who had no culturable bacilli at the time of operation.

The author concludes that (1) the risk of the emergence of resistant organisms has been exaggerated; (2) that operation should be performed after about 4 months' multiple drug therapy in those whose sputum still contains culturable bacilli; (3) that if the patient's sputum has become non-infectious, operation should be delayed until about 4 months after the sputum has become so, but if the disease was cavitated, 10 months should be allowed to elapse after the last positive culture. *F. H. Young*

FOX, W. & SUTHERLAND, I. **A Five-Year Assessment of Patients in a Controlled Trial of Streptomycin with Different Doses of Para-Aminosalicylic Acid in Pulmonary Tuberculosis.** *Quart. J. Med.* (n.s.) 1959, Jan., v. 28, No. 109, 77–95, 1 fig.

The standard of work in the Medical Research Council trials of antimicrobial drugs has received world wide approbation and the present trial has maintained this level. It reports the results at the end of 5 years on 115 patients who were treated for 3 months with 1 gm. of streptomycin daily, and varying doses of PAS. 42 patients received 20 gm. of PAS (sodium) (SP 20 series), 39 10 gm. PAS (SP 10 series), and 34 had 5 gm. PAS daily (SP 5 series). The patients all had extensive bilateral acute tuberculosis.

At the end of the 3 months the further treatment was left to the clinician in charge. Additional chemotherapy of some kind was given to approximately 70% of the patients, but according to present standards it was usually inadequate. Some form of collapse or resectional therapy had been given to 62–69% of the survivors at the end of 5 years. In both cases there was little difference between the numbers in each of the PAS categories. At the end of 5 years, 19% of SP 20, 26% of SP 10 and 21% of SP 5 series had died

of pulmonary tuberculosis; the disease was assessed as arrested or quiescent in 66%, 45% and 62% of the 3 groups. 32%, 34% and 19% of the survivors of the groups had not returned to work. Bacilli resistant to streptomycin were recovered from 6 (15%) of SP 20, 13 (35%) of SP 10, and 17 (52%) of the SP 5 series. The likelihood of the development of resistant strains was much greater in the presence of large cavities.

In the whole series the following features as assessed on admission to the trial were associated with an unfavourable prognosis: extensive cavitation, high pyrexia and a high erythrocyte sedimentation rate; additionally, failure of the above to respond to treatment promptly was likely to lead to a poor result. Although there was an appreciable statistical difference between the prospect of the emergence of resistant organisms between the 3 dosage schemes, it was found that the effect on prognosis of this was associated far more with persistence of large cavities than the presence of the resistant organisms.

As by modern standards the antimicrobial treatment was inadequate, much better results can now be expected.

[See also this *Bulletin*, 1956, v. 31, 998, for earlier studies by the authors.] *F. H. Young*

LEIFHEIT, H. C. & SMITH, Elizabeth R. B. **Quantitative Estimation of Isonicotinic Acid Hydrazide and p-Aminosalicylic Acid in Blood Serum.** *Amer. J. Clin. Path.* 1959, Feb., v. 31, No. 2, 142–7, 4 figs.

"A quantitative chemical method for the determination of free Isoniazid (INH), total Isoniazid (INH), and *p*-aminosalicylic (PAS) acid in blood serum has been evaluated, simplified, and presented in detail. Inasmuch as some patients are "stronger acetylators" than others, the technic for total INH (Free INH plus Acetyl INH) has been included, as has that for PAS. In routine use, however, the determination is usually limited to levels of Free INH.

"The limit of error of the method for free INH is taken as '±0·5 gamma per ml.' Several items of nonexpensive and improvised apparatus are described. Among them, centrifuge tubes with polyethylene snapcaps have been introduced. Their use is recommended because of the nonfreezing and nonbreakable properties of the stopper, as well as the low cost of the combination."

BERTE, S. J., LEIFHEIT, H. C., DEWLETT, H. J. & TUCKER, E. B. **A Critical Analysis of the Accuracy of a Chemical and Biologic Method of determining Serum-Free Isoniazid.** *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 344–50.

BENIANS, R. G. & PINTO, C. J. **A Fatal Case of Viomycin Hypersensitivity.** *Brit. J. Tuberculosis.* 1958, Oct., v. 52, No. 4, 325–7, 3 figs. on pl.

"A case is recorded of renal damage, fever and drug rash following twice weekly viomycin treatment. At post-mortem the renal tubules showed necrosis."

STEENKEN, W., Jr., MONTALBINE, V. & THURSTON, J. R. **The Antituberculous Activity of Kanamycin *in vitro* and in the Experimental Animal (Guinea Pig).** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 66–71.

Kanamycin was isolated from *Streptomyces kanamyceticus* in 1957, and YANAGISAWA and SATO (*J. Antibiotics*, Ser. A, 1957, v. 10, 233) described its activity against tubercle bacilli which are both susceptible and resistant to streptomycin. This is confirmed in the present study, and also that it is active against a photochromogenic strain. The authors found that the substance was active against bacilli resistant to any one of the common antimicrobic drugs except neomycin and viomycin. Resistance could be induced rapidly after 4 transfers in Tween-albumin medium containing the drug. On guineapigs there was no noticeable toxaemia to dosage of 10 to 40 mgm. per kgm. of body weight, but an increase of dosage gave rise to toxic symptoms. *F. H. Young*

WRIGHT, K. W., RENZETTI, A. D., Jr., LUNN, J. & BUNN, P. A. **Observations on the Administration of Kanamycin to Patients with Tuberculosis.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 72–7, 2 figs.

Following the demonstration that kanamycin was active against tuberculosis in guineapigs and not toxic, the authors tried it on 11 patients whose sputum contained tubercle bacilli, and 1 with photochromogenic acid-fast bacilli. 11 patients had far advanced disease of long duration, and the age range was 40 to 67 years. 8 were treated with kanamycin alone and the other 4 had various combinations (excluding streptomycin). 10 patients underwent treatment for 4½ to 6 months, and in 2 it was discontinued after 2 and 6 weeks respectively. The dosage was usually 0·5 gm. daily intramuscularly. Toxic phenomena were mild cylindruria without other signs of urinary irritation, and hearing loss in 2 patients, but no vestibular or haematopoietic disturbance. Eosinophilia was common, but only 1 patient had pruritus which disappeared in spite of continuation of treatment. In the 10 patients in whom treatment was continued, resistance of the bacilli rose from susceptibility to less than 10 μgm. to resistance to more than 100 μgm. per ml. Therapeutically the effect was thought to be greater than would be expected from rest and hospital care; 1 patient had sputum conversion.

The blood concentration was not significantly higher in the few patients who received 1 gm. daily than in those who received 0·5 gm.

It is concluded that the drug has some antituberculous activity in human patients. This is a small but carefully conducted trial. *F. H. Young*

SOMNER, A. R., ROSS, J. D., MACLEOD, H. M., STEWART, S. M., HORNE, N. W. & CROFTON, J. W. **"1314" in Pulmonary Tuberculosis.** *Brit. Med. J.* 1959, Feb. 21, 486.

This is a short preliminary report from the Department of Tuberculosis at Edinburgh on the use of the

drug "1314", alphaethyl*iso*nicotinic thioamide. 7 patients were treated with 1 gm. daily, together with 4 gm. tetracycline which has little antituberculous activity but is valuable in delaying the development of resistant organisms. All had organisms resistant to the standard drugs.

In 1 patient the sputum previously positive for 7 years became negative. 1 patient became intermittently positive but did not develop resistant organisms. In 4 patients the sputum remained positive and resistant organisms appeared after 5, 7, 8 and 18 weeks' treatment. The last patient had resistant organisms after 3 weeks, and died 3 weeks later. Drug intolerance was troublesome (nausea and vomiting) and frequently led to the suspension of treatment.

The authors conclude that the drug is effective, but should not be used normally pending the results of controlled trials. *F. H. Young*

RIST, N., GRUMBACH, Francoise & LIBERMANN, D. **Experiments on the Antituberculous Activity of Alpha-Ethyl-Thioisonicotinamide.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 1–5. [18 refs.]

The compound thioisonicotinamide was first synthesized in 1952, but tests suggested that *in vitro* it was 400 times less active than isoniazid. In 1954 some evidence appeared that it was active in experimental tuberculosis in mice, and this occurred against isoniazid resistant organisms. It appeared to be useful in leprosy, and these contradictory results led to the idea that the substance underwent changes in the body. An alpha-ethyl derivative was produced (1314Th) which was less toxic but 4 times more active.

It is claimed that this compound was inhibitory for *Mycobacterium tuberculosis* in concentrations between 0·6 and 1·2 μgm. per ml. in fluid media, and 2–4 times greater than this on solid media. In mice the protective dose was 12 mgm. per kgm., when treatment was postponed for 14 days its effect was as rapid as isoniazid and more so than streptomycin. In guinea-pigs it was found to be twice as active as streptomycin. Resistance developed rapidly when 1314Th was used alone, but when streptomycin or isoniazid were added this did not usually occur. Cross resistance to isoniazid or any of the commonly used drugs did not occur. The acute toxicity in mice was only one-fifth of that of isoniazid. *F. H. Young*

BROUET, G., MARCHE, J., RIST, N., CHEVALLIER, J., & LEMEUR, G. **Observations on the Antituberculous Effectiveness of Alpha-Ethyl-Thioisonicotinamide in Tuberculosis in Humans.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 6–18, 1 fig.

In a clinical trial alpha-ethyl-thioisonicotinamide (1314Th) was given in doses of 1 gm. per day with varying spacing of administration to 102 patients. Of these 78 were treated for at least 3 months; the reasons for suspension of treatment in the 24 included 5 suspended for intolerance, and 3 for lack of response at the end of 2 months. Of the 78, 43 had apparently recent, and 35 chronic, disease.

In the recent group, 23 had 1314Th alone, and 20 had other microbial drugs as well, and in the chronic group 3 and 32 respectively.

There was appreciable gastro-intestinal intolerance, which often led to loss of weight, but not marked toxicity. This was classified as severe or very severe in 36 patients. No major toxic effects were noted. The maximum routine dose is apparently 15 mgm. per kgm.

Clinical and radiological results are rather indeterminate owing to the comparatively small number of patients, the fact that treatment was usually for 3 months only and the concurrent use of other antimicrobial drugs. Of the 23 patients treated with 1314Th alone, considerable clinical improvement was noted, especially in patients who had little or no gastro-intestinal upset. Radiologically substantial improvement was noted in 8 out of 23 patients. In 9 out of 20 patients treated with 1314Th and isoniazid similar improvement was noted. In 4 out of 26 patients with chronic disease treated with 1314Th and other antimicrobials substantial radiographic improvement was noted.

Bacteriologically 80 out of 83 strains of bacilli were sensitive at the commencement to 1314Th, and there was no cross resistance to isoniazid. Of 18 positive sputum cases, 7 were still positive at the end of 3 months. On the drug alone resistance develops quickly, in some cases at the end of 2 months. When 1314Th was given with isoniazid 17 out of 19 patients had sputum conversions.

The authors conclude that a good case has been made out for the use of 1314Th in conjunction with other antimicrobials, but its use alone is not justifiable. *F. H. Young*

LÉVI VALENSI, A. & MOLINA, C. Le traitement des tuberculeux pulmonaires en dehors de l'hôpital et du sanatorium. [**The Treatment of Pulmonary Tuberculosis outside Hospital**] *Maroc Méd.* 1958, July, v. 37, No. 398, 748–60. [Numerous refs.]

There is as yet no universal agreement about the desirability of treating pulmonary tuberculosis outside hospital and it has been objected to on 2 main grounds.

The first objection considered by the authors is that there is danger that those who remain in contact with the patient may be infected by him and that the infecting organisms may be drug resistant. In reply to this it is stated that isoniazid-resistant tubercle bacilli show diminished or no virulence [in experimental animals] and may fail to grow on culture; moreover there are few instances of such organisms having been found to cause disease in man.

Some authors have reported an increased incidence of primary infection in young children in France since the introduction of extra-hospital treatment, and in some series published 40% of the primary infections evidenced by tuberculin conversion were considered to be due to infection by patients being treated with isoniazid alone or combined with other drugs. On the

contrary other workers have reported a marked reduction of primary infection in the contacts of patients undergoing treatment outside hospital.

The present authors studied 200 families in contact with a member suffering from pulmonary tuberculosis; in 100 homes where the patient received no chemotherapy the infection rate in the contacts was 13·5% and in 100 where the patient received chemotherapy it was 3%.

The next objection considered is that the patient will not rest properly. The authors admit that complete rest is necessary at the beginning of treatment but when improvement is established as shown by clinical, radiological and bacteriological examination full rest is not desirable and some activity is desirable.

The indications for extra-hospital treatment are essentially socio-economic but they are also medical. A short period of hospital treatment may be necessary followed by treatment at home. The most suitable combination of drugs is PAS-isoniazid but the authors have abandoned PAS because of its high cost and unpleasant effects in many cases. If PAS is used the combination named pasiniazid is recommended (para-amino salicylate of isoniazid).

Treatment may also be ambulatory, the patient carrying on his normal routine or domiciliary after a short stay in hospital or in a day sanatorium with return home at night.

Ambulant treatment was given to 2,315 patients from 1950 to 1956, at an Algerian centre; clinical, radiological and bacteriological cure was obtained in 20% of 1,780 adults, improvement occurred in 46% with sputum conversion in most, the disease was stabilized in 16%, and 18% became worse. The results in children were excellent. Domiciliary treatment following hospital resulted in improvement in 90% of the adults. The day sanatorium also gave good results, and should be extended.

It is recommended that specific drugs be supplied free to all who cannot afford them. There should be supervision to ensure that the regimen is followed and patients should be recalled to the clinic every 3 months. Full use of BCG should be made in contacts and chemoprophylaxis is recommended especially for children and adolescents whether reactors or non-reactors. The recommendation is 5–10 mgm. per kgm. of isoniazid by mouth every day for 3 months with a rest period of 3 months. *H. G. Calwell*

Acta Tuberculosea Scandinavica. 1959, v. 36, No. 4, 213–41. **Prognosis of Tuberculous Pleurisy. A Follow-Up of Cases discharged from the Ullevål Hospital during the Years 1926–45.**

This article deals with the probability that various forms of tuberculosis will develop after primary tuberculous pleurisy. All patients discharged from the Ullevål Hospital with a definite diagnosis were included under the headings,—primary tuberculous pleurisy (2,201), patients with a prior attack of pleurisy (73), patients thought probably to have non-tuberculous pleurisy (291); a total of 2,565 who were discharged in the 4 quinquennia 1926–30, 1931–5, 1936–40, and 1941–5. The first appendix gives details of information extracted from the records; it shows how the diagnostic criteria improved and deals with 2,201 patients. The difficulty of drawing correct conclusions from such a source is shown by the fact that definite lung infiltration occurred twice as often in the second quinquennium as in the others, owing to the reporting by a certain radiologist (reports had to be taken as films were not available for re-scrutiny). In about 90% of patients exudate was demonstrated. In the follow-up (which was made until death or 1954) 110 patients (4·3%) were lost sight of.

A table is given showing the actual death-rate per 1,000 per year by age and sex. The death-rate of all ages compared with the expected rate was 2·3 in males, and 2·5 in females, but in the first year after discharge was 7 times the expected rate. Where there was no tuberculous disease for 5 years after discharge the rates were 1·4 and 1·5 respectively. For all ages the morbidity of any type of tuberculosis was 45 per 1,000 in the first year after discharge. For primary tuberculosis the morbidity was about the same, but there was a relatively small difference between the first 2 quinquennia after discharge.

As might be expected there was a considerable excess of cases of tuberculosis where there was a family history, but in the age-group 5 to 9 years the occurrence of a family history was considerably higher in males and after 10 the figures were reversed.

The figures for extrapulmonary tuberculosis are given; the numbers are small but they illustrate the relatively late occurrence of genito-urinary tuberculosis.

[This is a most careful and meticulous statistical study. Great care has been taken to exclude where possible extraneous factors, though the accuracy of the data on which it is founded must sometimes be suspect, especially the interpretation of the X-rays. Like all these long term studies the conclusions are more of historical value owing to the revolution of prognosis by the introduction of antimicrobial drugs; but as presented it is difficult to find anything to criticize.] *F. H. Young*

Gray, N. J. & Taft, L. I. **Aspiration Liver Biopsy in the Diagnosis of Miliary Tuberculosis: Report of a Case.** *Med. J. Australia.* 1959, Jan. 17, v. 1, No. 3, 79–80, 3 figs. (2 on pl.) [17 refs.]

This is an account of a case in which the cause of a pyrexia of unknown origin was discovered by liver biopsy.

A man aged 45 years who had no history of contact with tuberculosis was examined in April 1957 because of 3 weeks' pyrexia (100–104°F.). He complained of abdominal pain, headache, cramps in legs and transient diarrhoea. Penicillin had been given without effect. Although the patient was very ill all examinations gave negative results. Various antibiotics were given including streptomycin, for 2 days only, but no clinical improvement was seen.

On the 31st day of the illness the man was severely ill and drowsy with a temperature of 105°F. No abnormal physical signs were detected in the lungs but a skiagram showed very fine nodulation suggesting miliary tuberculosis. Tubercle bacilli could not be

found anywhere. Liver puncture was done 24 hours later and histological examination of the tissue showed typical tuberculous granulomata with acid-fast bacilli. A culture of *Mycobacterium tuberculosis* was obtained after 14 weeks' growth.

Treatment with streptomycin, isoniazid and cortisone was begun at once with resulting immediate and continuing improvement. Tuberculin sensitivity of the skin was absent until the 8th week of treatment when a weak reaction to 100 TU of OT was obtained.

Liver biopsy was repeated after 2 months when granulomata were seen but no bacilli and at 7 months when healing granulomata were seen. No bacilli were detected and culture was negative. 6 months after the onset of the illness the patient began light work on maintenance chemotherapy and was in excellent health when last seen 4 months later. *H. G. Calwell*

MISRA, S. S., SAXENA, K. M. & MISRA, R. M. **Levinson's Test in Tuberculous Meningitis.** *J. Indian Med. Ass.* 1958, Dec. 16, v. 31, No. 12, 480–83.

Levinson's test, although described in 1929, does not seem to have had a favourable reception. It is used as an adjuvant test in the diagnosis of tuberculous meningitis. Briefly the test consists of adding 1 cc. of cerebrospinal fluid to 2 tubes containing 1 cc. of 3% sulphosalicylic acid solution and 1% mercuric chloride solution respectively. If at the end of 24 hours the precipitate in the mercuric chloride tube is more than twice that in the sulphosalicylic acid tube the test is positive.

The authors report that in 15 non-meningitic patients and in 5 patients with pyogenic meningitis the test was negative. In 111 patients with tuberculous meningitis (1 should be excluded as there was no precipitate) the test was positive, as defined, in 91 (82%). [The figures for each patient are given in a table but the abstracter cannot confirm this figure from the table.] In 3 patients the test previously negative became positive later. Usually, but not invariably, the M/S ratio tended to fall and finally became negative as the patient improved, and this was of value in determining the length of treatment. The authors think that the M/S ratio tended to be higher in severe cases.

F. H. Young

REILLY, Lilian V. **Miliary and Meningeal Tuberculosis: a Review of 354 Cases.** *Ulster Med. J.* 1958, Nov. 1, v. 27, No. 2, 146–57.

The 354 patients who are the subject of this review were treated in a hospital in Northern Ireland from late in 1947 when streptomycin first became available until the end of 1956; 114 (32·2%) died. There were 76 with miliary disease alone, 160 with meningitis and 118 with both combined.

The largest group (120) was aged 0–4 years, the smallest (33) 10–14 years and there were 95 patients aged 20–66 years with 5 over 60. 60% of the adults were aged 20–30 years.

The highest death-rate was in the youngest group, and 60% of all deaths occurred within 1 month of admission. The number of patients with advanced disease was high in all 3 disease groups and at all ages.

Prodromal symptoms were variable in duration and degree. History of contact with an infectious tuberculous patient was obtained in many cases but frequently the infector was not discovered until after the patient's admission to hospital. There were several instances of 2 or 3 members of a family having miliary or meningeal disease at the same time.

Radiological evidence of an intrathoracic primary tuberculous focus was found in 109 patients (30·7%), and evidence of an extrathoracic focus was found in a few. There was a history of erythema nodosum in less than 10 patients. Evidence of abdominal tuberculosis was also very rare.

Previous clinical tuberculosis was commoner in adolescent and adult groups than in children; there were only 36 such cases—bone, genito-urinary or glandular. Pulmonary tuberculosis of adult type was found in only 52 patients.

There were slightly more females than males with miliary disease the excess being at ages 0–4 and 15–19 years. Other authors have noted this tendency.

The Mantoux reaction was almost invariably positive in the miliary patients. *Mycobacterium tuberculosis* was recovered by culture from the gastric residue in 49 of the 76 patients. The diagnosis was usually supported by the X-ray findings and the detection of choroidal tubercles.

The diagnosis of meningitis was made by the examination of the cerebrospinal fluid. A falling sugar level was considered to be an important diagnostic feature. The specific organism was isolated by culture of the cerebrospinal fluid in 142 cases (88·7%) and from the gastric residue in 40 of 160 (25%). Choroidal tubercles were found in only 8 patients with meningitis alone.

Of the 118 patients with combined miliary and meningeal disease 64 had both conditions on admission, and meningitis developed later in 54. The development of meningitis became less common after PAS began to be used, and no patient developed meningitis while actually under treatment with streptomycin, PAS and isoniazid combined.

Treatment changed greatly during the period; 50% of the patients with meningitis died on treatment with streptomycin, 35% with streptomycin and PAS and 25% when isoniazid was added to the régime. Intrathecal streptomycin was given to the majority of patients with meningitis but it was later omitted in many cases without detriment.

The most serious complication was severe mental retardation usually with blindness and deafness; 11 of 178 patients with meningitis were so affected. Deafness occurred in 24, ataxia in 22, blindness in 16 and mental retardation in 19. There was relapse in 28 patients, 8 of whom died.

The paper ends with the cheerful statement that whereas in 1950 62 patients with miliary or meningeal tuberculosis were admitted to the hospital, in 1957 the number had fallen to 17. *H. G. Calwell*

LORBER, J. **Freeze Dried BCG Vaccination of Newborn Infants by the Multiple Puncture Method.** *Tubercle.* 1959, Feb., v. 40, No. 1, 21–5, 1 fig. [17 refs.]

BCG vaccination by intracutaneous injection gives excellent results but the technique requires skill and because of the frequency of complications some physicians are reluctant to vaccinate infants.

The frequency and the extent of the local complications may be reduced by the use of freeze-dried vaccines, and attempts have been made to eliminate them by using a percutaneous, multiple puncture technique of vaccination.

As part of a series of clinical trials with freeze-dried vaccine of British manufacture [this *Bulletin*, 1956, v. 31, 903; 1957, v. 32, 1146;, 1958, v. 33, 572] it was decided to use the multiple puncture method. A vaccine was prepared in a medium containing dextran which when reconstituted with water formed a sticky fluid suitable for the purpose. It was approximately 50 times stronger than the vaccine used for intracutaneous administration.

The subjects chosen for vaccination were healthy infants who were not in known contact with persons with active tuberculosis. They were all vaccinated within 8 days of birth without preliminary tuberculin testing. The Heaf gun was used at the 1 mm. setting and applied over a drop of reconstituted vaccine; 2 insertions of the needles were made with a slight rotation of the apparatus between them. After vaccination the vaccine was allowed to dry on the skin.

240 infants completed the post-vaccinal tests. The vaccination lesions were inconspicuous in all, consisting of 4–12 papules 1 mm. in diameter. There was no ulceration suppuration or regional adenitis.

115 of the 240 infants had a post-vaccinal tuberculin jelly test, of whom 44 (38%) showed a reaction 6 to 8 weeks after vaccination. Of the 71 non-reactors and the 125 infants who had no jelly test 186 (95%) reacted to the Mantoux or Heaf tests, 1 was negative to 10 TU and 9 (4%) to 100 TU of OT. Thus 230 of the 240 (95·8%) underwent tuberculin conversion 6 to 8 weeks after vaccination.

The 10 non-reactors were retested with 100 TU 3 to 4 months after vaccination; 4 reacted strongly and 6 remained negative. By this stage, therefore, the conversion rate was 97·5%.

The absence of complications and the high conversion rate speak well for this method of vaccination. There is, however, no knowledge yet about the duration of allergy or immunity and it will be necessary to follow this group for several years and to study larger groups composed of different age groups. *H. G. Calwell*

SPARROW, H. & CARRÉ, G. Conseils pour la pratique de la prémunition contre la tuberculose par le B.C.G. —Buccal. [**BCG Vaccination by Mouth**] *Arch. Inst. Pasteur de Tunis.* 1958, Sept.–Dec., v. 35, Nos. 3/4, 307–13.

The Brazilian method of oral BCG vaccination has been studied in Tunis since 1953 and found to be efficacious and safe.

It was the practice to give 6 doses of vaccine at intervals of a fortnight, *viz.* 50 mgm. per dose up to the age of 6 months and 100 mgm. between the ages of 6 months and 5 years. Difficulty in following this routine to its completion led to the number of doses being reduced, and the results of giving a single dose of 50–100 mgm. to children aged 7 days to 7 years are tabulated in the paper.

Of 63 children aged less than 2 years only 2 failed to develop tuberculin sensitivity, but of 50 aged 3–7 years 24 failed to do so. This failure rate of about 40% is ample proof of the uselessness of a single dose of vaccine for children over 2 years of age. On the contrary even a single dose will afford protection to young infants, but it is emphasized that a second dose must be given in the course of the next or second year. The protection thus assured will be consolidated by later revaccination by scarification or intracutaneous injection on entry to school or during school life.

Every vaccinated child should have a post-vaccinal tuberculin test which should be repeated for those entering school and yearly thereafter for those displaying absence of tuberculin sensitivity the previous year.

BCG vaccination differs from those vaccinations which act by the production of antibodies in that it is a form of premunition which depends on the persistence in the body of living bacilli. In the authors' experience the most favourable time for the development of premunition is in the child's earliest life since later on BCG is eliminated rapidly by the body's defences with consequent failure of premunition against virulent tubercle bacilli to develop.

Vaccination against tuberculosis is recommended for the youngest children and preferably by the oral method because of its simplicity, acceptability and the absence of complications which may follow intracutaneous vaccination. Infants should be vaccinated as soon as they reach their birth weight unless they are premature or ill.

The vaccine should be given on an empty stomach by dropping it from a pipette into the mouth, and the child may be made to swallow if sweetened water is given. All should be done gently and the child kept at rest for several minutes after the vaccine has been swallowed. *H. G. Calwell*

PARROT, L., CATANEI, A. & LAVERDANT, C. Sur un essai de vaccination antituberculeuse itérative. [**A Comparison of Post-Vaccinal Allergy in Infants Vaccinated with BCG by Scarification and Repeated Oral Administration**] *Arch. Inst. Pasteur d'Algérie.* 1958, Sept., v. 36, No. 3, 297–303. [12 refs.]

The object of this investigation, which was made in Algeria, was to compare post-vaccinal allergy after 2 different methods of vaccination, *viz.* scarification and repeated oral administration. The second method is usually described as the Brazilian method of DE ASSIS [this *Bulletin*, 1954, v. 29, 603].

Instead of the tuberculin test the authors used a BCG test in which the skin is scarified through a drop of heat-killed BCG vaccine containing 75 mgm. of organisms per cc.

33 infants aged 2 months to 2 years, 9 white and 24 Negro, all non-reactors to the BCG test were vaccinated; 17 were given the vaccine by scarification on November 26 1955 and on the same day 16 were given

100 mgm. of BCG by mouth, which dose was repeated on December 15 and 29, 1955 and January 15 and 29, and February 15 1956—a total dose of 600 mgm. in about 3 months. No untoward incident occurred.

The infants in both groups were tested with BCG in April and November 1956, in April 1957 and in November 1958. During the 26 months of observation the reactor rate to BCG was 89·4% in those vaccinated by scarification and 82·6% in those vaccinated orally. The proportion of weak reactions was about the same in both groups.

As is usual in Algeria more positive reactions were seen in spring than in autumn and winter as weak sensitivity may disappear temporarily during the cold season. No case of anergy due to desensitization by repeated vaccination was seen.

The authors conclude that the method of De Assis is not superior to the other. They agree with Calmette and Guérin that there is no other form of acquired resistance to tuberculous infection, whether natural or provoked by BCG, than that which results from infection by the tubercle bacillus and corresponds to premunition. The authors comment that in the light of the results of the BCG reaction it can be said today that there is no immunity against tuberculosis without allergy.

[See also this *Bulletin,* 1952, v. 27, 648.]

H. G. Calwell

VENEREAL DISEASES

Durel, P. & Borel, L. J. De la syphilis sans chancre. Discussion du rôle des antibiotiques [**Syphilis without Chancre. Discussion on the Role of Antibiotics**] Reprinted from *Presse Méd.* 1958, Nov. 22, v. 66, No. 82, 1827–9, 6 figs. [14 refs.]

This little monograph sets out the views of 2 well-known French syphilologists. *Syphilis d'emblée* is an expression which has been greatly overdone and these authors agree with Fournier that it is extremely rare; in the female a primary lesion can nearly always be found if careful search is made especially in the vagina and cervix uteri; on the other hand it is accepted that in bejel (a form of syphilis) a chancre is rarely seen and syphilis in the mouse is normally latent.

This matter is of special importance in prostitutes, especially in France where they are examined regularly, and it has been estimated that in 40% of these the disease is discovered by serum tests.

The importance of antibiotics in syphilis should not be underestimated; they do not mask syphilis but they may delay its appearance. Most antibiotics have an action on spirochaetes but penicillin is far the most active, and subcurative doses may cause considerable delay in the appearance of physical signs; in the case of long acting preparations the serum level may fall after a time below the lethal dose and then spirochaetes will start to multiply. Benzathine penicillin G is useful as a prophylactic and a monthly dose of 2·4 mega units will protect against both syphilis and gonorrhoea.

The risk of allergic reactions is relatively small but it must be recognized that the gonococcus is becoming more and more penicillin resistant.

There is a great deal of wisdom contained in this article [but no mention is made of "transfusion" or "congenital" syphilis, in neither of which is a chancre likely to be found].

T. E. Osmond

Miller, J. L., Brodey, M. & Hill, Justina H. **Laboratory Studies in a Series of Biologic False-Positive Reactors.** *Arch. Dermat.* 1959, Feb., v. 79, No. 2, 206–10. Discussion 210–12.

This is one more contribution [this *Bulletin,* 1957, v. 32, 1044] to the subject of biologically false positive reactions (BFP) in tests for syphilis; 79 persons were investigated and 67 were apparently healthy while 12 were suffering from systemic diseases (these included rheumatoid arthritis, Laennec's cirrhosis, congenital haemolytic anaemia, cryoglobulinaemia, cerebral vascular accident, systemic lupus erythematosus, diabetes mellitus, brain tumour, polyarthritis, epilepsy and ? lymphoma).

In the first group serum tests for syphilis (STS) had been positive for 1–40 years (median 5) and in the second the median was 3 years; in the first group the ratio was 15 men to 52 women and in the second 1 man to 11 women; the average age was about 45. The results of the various tests carried out are set out in a table; the most important was an abnormal factor associated with gamma globulin; cephalin flocculation and thymol turbidity tests were positive in 30% of group I and 80% of group II; the sedimentation rate was increased in 24% of the former and in 7 out of 11 of the latter.

The authors recommend that if all the above tests are negative yearly observation is advisable; if some are positive they should be repeated at intervals.

In the discussion which followed it was stressed that continued observation was necessary in those patients who showed abnormal reactions but those who did not could safely be dismissed; one speaker called the phenomenon serendipity* [which is a new word to most of us] and thought that a solution depended on separating the globulins and dividing them into their component parts; others thought that the various treponemal tests, especially those using Reiter antigens, would help; an interesting idea was that a challenging injection of a highly purified killed treponemal suspension would often convert a doubtful TPI test to positive and so establish a diagnosis of syphilis.

T. E. Osmond

* "Serendipity. The faculty of making happy and unexpected discoveries by accident." *Concise Oxford Dictionary,* 1952.

Ranque, J. & Depieds, R. Intéret du test d'immobilisation des tréponèmes en milieu tropical. [**The TPI Test in the Tropics**] *Méd. Trop.* Marseilles. 1958, Nov.–Dec., v. 18, No. 6, 893–903. [13 refs.]

Classical serum tests for syphilis frequently give false positive results where tropical diseases are prevalent. The authors report their experience of carrying out

more than 7,000 TPI tests of which nearly 1,500 were done in the tropics; though this test does not distinguish between syphilis, yaws and bejel it does detect a treponematosis.

The test was carried out on persons suffering from such diseases as relapsing fever, leptospirosis, fusospirochaetosis, trypanosomiasis and sickle-cell anaemia and in animals experimentally infected with *Trypanosoma gambiense, T. brucei* and *T. equiperdum, Plasmodium berghei* and visceral leishmanioses

In numerous diseases including leprosy, virus infections, rickettsioses and parasitic diseases the authors found classical tests often positive or disagreeing while the TPI was negative; in a few this last was positive but in most such cases syphilis was certainly or possibly present as well; moreover these authors found numerous cases of undoubted syphilis where the classical reactions were negative and the TPI positive. A warning is issued that a positive TPI reaction merely indicates a past infection with treponemes but does not necessarily indicate active disease. The newer serum tests with cardiolipin antigen are less likely to give false positive reactions but it is always advisable to avoid taking blood specimens during the active stages of (tropical) diseases.

Numerous statistics are given of tests (TPI and classical) carried out by the authors in various diseases.

T. E. Osmond

GERTLER, H. Beitrag zum Problem der Penicillinresistenz der Gonokokken. **[Observations on Penicillin Resistance in Gonococci]** *Ztschr. f. ärztl. Fortbildung.* 1959, Feb. 1, v. 53, No. 3, 169–72. [21 refs.]

This paper describes the methods used for treating gonorrhoea at a clinic in Potsdam. In chronic and complicated cases these include the injection of Olobintin [a 40% solution of rectified turpentine in olive oil; details of administration are not given] to produce fever, as well as large doses of penicillin. Such methods almost eliminated treatment failures in "stationary" patients, but these continued in "ambulant" patients and were known in some cases and assumed in others to be due to re-exposure [in what sense the first group were "stationary" is not clear]. It is concluded that gonococci are not becoming penicillin-resistant [but no tests of the sensitivity of these strains were apparently carried out: such tests have shown elsewhere that strains exist with substantially increased degrees of resistance]. *L. P. Garrod*

KARLTORP, N. & LODIN, A. Tetracyklinhydroklorid och tetracyklinhexametafosfat vid behandling av ospecifik urethrit. **[Tetracycline Hydrochloride and Tetracycline Hexametaphosphate in the Treatment of Non-Specific Urethritis]** *Nordisk Med.* 1959, Mar. 19, v. 61, No. 12, 468–9.

The English summary appended to the paper is as follows:—

"Of 72 male patients with non-specific urethritis 29 were treated with tetracycline hydrochloride (Tetradecin, Astra) and 26 with tetracycline phosphate complex (Tetradecin novum, Astra). The dosage for both groups was 500 mg three times daily for three days. After five days 23 patients in each group were free from symptoms. At the same time only 1 of 17 untreated patients was symptom-free. With a microassay method therapeutically satisfactory quantities of tetracycline (>1 γ/per ml) could be measured in blood and urethral discharge in some cases. In the authors' opinion the tetracycline phosphate complex seems to be preferable."

FILADORO, F. & ORSI, N. **Cultivation of *Trichomonas vaginalis* on a Solid Medium and its application to the Assay of Trichomycin Potency.** *Antibiotics & Chemotherapy.* New York. 1958, Nov., v. 8, No. 11, 561–3, 2 figs.

The authors describe a method for cultivating *Trichomonas vaginalis* on solid medium, using a modification of CPLM medium described by TRUSSELL (*Trichomonas vaginalis and Trichomoniasis.* 1947. Springfield, Ill. Charles C. Thomas). For growth of surface cultures, 2% agar is added to CPLM, the medium is dissolved at 100°C., cooled to 50°C. and, after addition of 10% ox or horse serum and a solution containing penicillin (50 units/ml.) and streptomycin (50 μgm./ml.), the mixture is poured into Petri dishes. A culture of the flagellate (in CPLM) is then streaked on the surface of the medium, and the plates are incubated anaerobically at 37°C. for 48 hours in a desiccator containing CO_2. For submerged cultures the procedure is modified by addition to CPLM of only 1% agar and inoculation of the flagellate culture before the plates solidify.

For the quantitative assay of the potency of trichomonostatic activity of trichomycin, the following method was used. A layer of 1% agar inoculated with *Trichomonas* is poured on to a layer of CPLM containing 2% agar without serum, the resulting volumes for the two layers being 10 ml. and 20 ml. respectively. Then trichomycin, dissolved in phosphate buffer at *p*H 6, is placed on the agar in porcelain cups containing various concentrations of the antibiotic. The zones of growth inhibition appearing after 36–48 hours at 37°C. in an atmosphere of CO_2 are measured with a calibrator. *C. A. Hoare*

COSAR, C. & JULOU, L. Activité de l'(hydroxy-2'éthyl)-1 méthyl-2 nitro-5 imidazole (8.823 R.P.) vis-à-vis des infections expérimentales à *Trichomonas vaginalis.* **[Activity of (Hydroxy-2'Ethyl)-1 Methyl-2 Nitro-5 Imidazole (8823 R.P.) in Experimental *Trichomonas vaginalis* Infections]** *Ann. Inst. Pasteur.* 1959, Feb., v. 96, No. 2, 238–41.

The antibiotic 8823 R.P. was obtained as a result of studies on antibiotics derived from a strain of *Streptomyces;* its LD50 for mice is 4·3 gm./kgm. compared with 0·63 gm./kgm. for aminitrozole and 0·15 gm./kgm. for azomycin when given by mouth; when given daily over 5 days to mice the maximum tolerated doses were 2·5 gm./kgm., 0·2 gm./kgm. and 0·05 gm./kgm. respectively.

Rats were unaffected by a daily dose of 8823 R.P. of 50 mgm./kgm. over a month and dogs similarly by 100 mgm./kgm.

In vitro it was found that 1/400,000 8823 R.P., 1/75,000 aminitrozole and 1/25,000 azomycin killed 99% of organisms in 24 hours. *In vivo*, 1/200 of the LD of 8823 R.P. protected mice against a previous injection of *Trichomonas*; with aminitrozole half the lethal dose and with azomycin nearly a full lethal dose was necessary to achieve the same object.

It was found that in rats in 48 hours 13% of 8823 R.P. but only 0·2% of aminitrozole was eliminated in the urine. Döderlein's bacillus in culture was not inhibited by 1/300 8823 R.P. but was inhibited by 1/300,000 aureomycin.

[It will be interesting to see how far 8823 R.P. is effective in the treatment of trichomoniasis in human beings.]

T. E. Osmond

OTHER COMMUNICABLE DISEASES

The order of papers in this section is as follows: Tetanus; other diseases.

NEYMAN, K. & WOJDON, Halina. Tężec w województwie poznańskim w latach 1945–1956. [**Tetanus Cases in the Province of Poznan in 1945–1956**] *Przegląd Epidemiol.* Warsaw. 1958, v. 12, No. 2, 135–45, 4 figs. [13 refs.] English summary.

An analysis has been made of the incidence of tetanus in the province of Poznań, Poland, between 1945 and 1956, from data obtained from a questionary sent to all the hospitals in the province. Among a population of 2,172,112 there were 317 cases (1·4 per 10,000), and the incidence in individual districts ranged up to 4·4 per 10,000. Fewer cases were noted in the first half of the period, but this was probably due to defective documentation in the hospitals in the immediate post-war years. The main incidence occurred in the summer months, with a maximum in August and a minimum in March. Males predominated with 190 cases, and the highest incidence occurred in the 8–14-year age-group. Most cases were due to minor wounds, and there were 8 cases of neonatal and 7 of post-operative tetanus; 128 cases were fatal (40·37%).

D. J. Bauer

PATEL, J. C. & JOAG, G. G. **Dosage of Antitetanus Serum in the Treatment of Tetanus.** *Indian J. Med. Sci.* 1958, June, v. 12, No. 6, 438–9.

The results of treating 816 tetanus patients with 240,000 units antitetanic serum, 243 patients with 120,000 units, and 243 patients with 60,000 units are compared: the mortality was 40·44%, 34·57% and 39·92% showing that no statistical effect on mortality is produced by lowering the dosage. The authors refer to other work on dosage and feel that their clinical results accord with experimental findings. They feel that reduction of dosage to the lower amount is justified on clinical and economic grounds.

A. B. Christie

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order: General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; Others.

For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

WUNDT, W. Die Epidemiologie der Brucellose in Württemberg. [**Brucellosis in Württemburg**] *Arch. f. Hyg. u. Bakt.* 1959, Feb., v. 143, No. 2, 145–52, 1 fig. [10 refs.]

The author first points out that while in Scandinavian countries brucellosis is seldom found, in the Federal German Republic, there is a tendency to a larger number of cases and an ever wider distribution. A table giving the notified human cases in Germany from 1936–54 (those from 1947 refer only to the Federal German Republic) and for Württemburg shows that since 1947 there has been a gradual increase in numbers for both and, since, they refer only to notified cases and the diagnosis in chronic cases is difficult, these numbers are minimal.

Formerly in Württemburg *Brucella abortus* was the only cause of human and animal brucellosis, except for a few outbreaks of *Br. suis* infection in swine, but at the end of the last war sheep which had been pastured in northern France, where *Br. melitensis* is common, returned to the Pfalz region (which serves as winter pasture for sheep flocks in S. and S.W. Germany) and *Br. melitensis* infection spread from there to Hesse, Württemburg, and the right bank of the Rhine, *Br. melitensis* being isolated by the author from human blood culture and cow's milk in 1955 [this *Bulletin*, 1955, v. 30, 312].

The results of absorption tests on cases of human and animal brucellosis carried out at the Institute of Hygiene, Tübingen, from 1954 to 1958 show that out of 66 human cases of brucellosis, 39 were due to *Br. melitensis*, the source being cattle in 5 and sheep in 23, with 12 unknown (1 had both cattle and sheep).

A *Br. melitensis* infection is a more dangerous human disease, and man seems to be more sensitive to it than to *Br. abortus*.

The author recommends (1) that all possible use in special laboratories must be made of the most modern methods for the diagnosis and typing of brucellae; (2) all available steps must be taken to prevent *melitensis* infection in cattle particularly since the infection is so widespread in sheep; (3) individual cases when diagnosed must be notified at once so that the requisite preventive measures can be taken.

[Increasing attention is being paid on the Continent to the possibility of the transmission of *Br. melitensis*

from sheep to cattle and the consequent greater risk to man.] *W. K. Dunscombe*

GUDOSHNIK, A. N. **The Part played by Free-Living Ticks and by Rodents in the Circulation of** *Brucella. J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1299–305, 1 diagram. [Translated from Russian.]

The author points out that there are records of 60 species of wild vertebrates which have been shown to be susceptible to infection by *Brucella* and that 10 strains have been recovered from 40 species of animals. Also 17 species of ticks have been shown to be susceptible and natural infection found in 12 species. The present investigation was carried out to ascertain the importance of persisting infection in rodents and ticks in areas where eradication of brucellosis from domestic animals was being contemplated. The author established the presence of *Brucella* in house mice and in *Dermacentor marginatus* from farm animals and in fasting *D. pictus* from pastures. The infection was transmitted from both to guineapigs and from *D. marginatus* to a lamb. Evidence of transovarian transmission of *Brucella* in ticks was obtained. The author claims that the *Brucella* isolated from naturally infected ticks were identified as *Brucella melitensis* [details of identification of the species are not given]. The author reasonably recommends that attention should be paid to rodent extermination and disinsectization in foci where cattle, sheep and goats have been known to be infected with *Brucella.* *Frederick J. Wright*

LJUNG, O. **The Diagnosis of Tularaemia. With particular reference to Difficulties presented by Atypical, Abortive and Asymptomatic Forms of the Disease.** *Acta Med. Scandinavica.* 1959, Mar. 4, v. 163, No. 3, 243–9, 6 figs.

Although *Brucella tularensis* may be obtained on occasion by culture from the blood, lymphatic glands or other tissues, cultures from patients with suspected tularaemia are frequently negative. Therefore diagnosis in this disease of protean manifestations may depend largely on a correct interpretation of an intradermal test and agglutination tests. A positive intradermal test with inactivated *Br. tularensis* is a sure indication of present or former tularaemia. Variable results of agglutination tests with different suspensions necessitate a cautious interpretation being made. If initially a patient exhibits a negative agglutination test and rising titres follow, this supports a diagnosis of tularaemia. A moderate titre which does not increase is indicative of recent tularaemia but is against active disease. Illustrative examples are given.

[See also this *Bulletin*, 1958, v. 33, 1132.]

Frederick J. Wright

SHARP, C. F. **Laboratory Diagnosis of Leptospirosis with the Sensitised-Erythrocyte Lysis Test.** *J. Path. & Bact.* 1958, Oct., v. 76, No. 2, 349–56.

The author made a further evaluation of the sensitized-erythrocyte lysis (SEL) test for the detection of leptospiral antibody in human cases of leptospirosis. The test is essentially genus-specific and is therefore facultatively most useful in areas where a wide range of leptospiral serotypes is present. [For references to earlier work and techniques see papers by MCCOMB *et al.* and by CHANG *et al.*, this *Bulletin*, 1957, v. 32, 998.]

Sensitizing substance derived from cultures of *Leptospira australis A* was used to detect active infections due to the numerous serotypes present in Queensland, Australia. The first part of the investigation was made with paired sera (taken respectively during the febrile period and in convalescence) from 104 patients proved by culture to be suffering from leptospirosis. Rising titres were obtained in all cases. Of 84 cases in which the first serum was negative, the titres in the second samples ranged from 1/10 to 1/10,240. In the remaining 20 cases the first specimens had positive titres but the second specimens all showed 4-fold or greater rises in titre.

Paired sera from 90 patients in which the diagnosis was confirmed by rising agglutinin titres were next examined. Sera from 86 patients showed a rise in titre in the SEL test, 1 had a stationary titre and 3 gave negative reactions with both samples.

To investigate the specificity of the test, paired sera were tested from 198 patients with febrile illnesses but negative agglutination reactions for leptospirosis. 182 cases (92%) had negative SEL tests, 14 (7%) had stationary titres of 1/10–1/160 and 2 (1%) had titres rising from zero to 1/40. Tests were also made on 100 (single) sera submitted for routine antenatal Wassermann tests. 8 gave positive SEL reactions and, of these, 2 also had positive agglutination reactions.

In discussing these results the author states that there seems to be no explanation for the occurrence of stationary SEL titres in about 6% of healthy persons and of those suffering from fevers not due to leptospirosis. This complicates the interpretation of the results of the test, but even so it is a useful screening method especially in areas where many serotypes are present and recurrent outbreaks entail the laboratory examination of paired sera from many individuals.

J. C. Broom

See also p. 635, DESOILLE, MOLLARET & KOLOCHINE-ERBER Sur l'indemnisation des leptospiroses d'origine professionelle [**Compensation for Leptospirosis of Occupational Origin**]

BEAUDETTE, F. R. [Edited by.] **Progress in Psittacosis Research and Control.** With a foreword by R. E. SHOPE. pp. xii + 271, numerous figs. [Numerous refs.] 1958. New Brunswick: Rutgers University Press, New Jersey, U.S.A.

In 1953 a symposium on psittacosis was held in New York under the auspices of Rutgers University and its proceedings, published in book form, provided a valuable *mise-au-point* of the subject at the time. Since then, however, considerable progress has been made in several aspects of psittacosis research and a second symposium has been thought worth while after a lapse

of only 3 years. Here again the report of the proceedings takes the form of a book—*Progress in Psittacosis Research and Control*—and it is sad indeed that Dr. F. R. BEAUDETTE who organized both symposia and edited the first volume should have died before he had concluded the second. This new volume, which incidentally is beautifully produced, is divided into 4 parts: *Ecologic Factors in Disease*; *Diagnosis of Psittacosis*; *Psittacosis Therapy*, and *Progress in Control*. As one might expect from its title the first section is broader in its outlook than the other 3, at any rate this is true of the first 3 contributions which are concerned with general problems of viral infection and disease. In the first of these: *Infection into Disease* (pp. 3–12), R. J. DUBOS argues most convincingly that the general state of the host at the time of infection, a state which is dependent on so many factors, plays just as great a part as those more orthodox factors—virulence of parasite and immune state of host—in determining the course of the infection. R. J. HUEBNER in *Some Implications of New Information on Viral Infection* (pp. 13–18) draws attention to the quite staggering extent of silent virus infection which modern technique is revealing; he discusses its possible consequences in terms of degenerative disease and R. E. SHOPE in *Virus Reservoirs* (pp. 19–23) has something intriguing to say on this subject. The rest of Part I is more directly concerned with psittacosis. *Infections in Mammals Caused by Members of the Psittacosis Group of Viruses* (pp. 24–31) by J. A. BAKER reviews these diseases and mentions that 8 species, including the dog, are now known to act as natural hosts. The author also points out how the tissue tropism, which is such a feature of these agents, might be turned to advantage for the purpose of immunization. As an example of this he cites the *injection* of the cat with feline pneumonitis virus, which when so introduced multiplies without producing disease, but immunizes against a disease-producing infection which is *inhaled*. The remaining 2 communications deal with the epidemiology and ecology of psittacosis. J. H. STEELE and and J. H. SCRUGGS in *The Epidemiology of Psittacosis, 1951–1956* (pp. 32–51) give the facts and figures for what has been happening in America during these years. Parakeets and turkeys were responsible for most of the 1,733 human infections; less than 10% were caused by other birds; the solution of the human psittacosis problem in the United States depends on the control of the disease in these 2 categories of bird. The *Ecology of Avian Psittacosis, Particularly in Parakeets* (pp. 52–86), the concluding article in Part I, is contributed by Dr. K. F. MEYER and Dr. B. EDDIE. This is a subject which one might say they have made their own. It is an extremely valuable contribution and it is followed by a discussion with other members of the symposium which, incidentally, enables Dr. Meyer to contribute still further from his vast knowledge of the subject.

Part II is devoted to the diagnosis of psittacosis and some of it makes rather disappointing reading. Where it is a case of diagnosing infection in the bird the situation has not changed very much; it is still a question of post-mortem appearances and the demonstration of the infective agent by microscopy and by isolation, with serology as an occasional aid. It is true that in the case of the turkey, as D. E. DAVIS and J. P. DELAPLANE point out in their paper on *The Lesions of Ornithosis in Turkeys* (pp. 89–110), the post-mortem appearances differ from those seen in other species of bird. In the turkey the striking thing is the presence of caseo-fibrinous exudates on pericardium, liver, peritoneum and in the air sacs; but the virus is usually present in abundance in these exudates. There is the possibility too of help from an intradermal test in the investigation of ornithosis; A. A. BENEDICT in his (pp. 127–38) communication: *Intradermal Test for Detection of Ornithosis Exposure in Chickens and Turkeys* gives an account of his work on this promising test; he makes use of a soluble antigen of which he claims to have isolated 2. In the case of human infection, however, successful chemotherapy may annul or interfere with antibody response thus detracting from the value of serology in diagnosis. For this and other reasons, such as anamnestic response seen in brucellosis or Q fever. I. GORDON, in *The Diagnosis of Human Infection* (pp. 139–160), stresses the importance of persisting with the complement-fixation test to the extent of even a third specimen 6 to 8 weeks after infection, where clinical and epidemiological findings suggest psittacosis. The antigen used in the complement-fixation test continues to be a group antigen, in fact in the paper on *Ornithosis Complement Fixation Antigens from Infected Yolk Sacs* (pp. 117–26) its authors, M. VOLKERT and P. M. CHRISTIANSEN openly doubt the existence of a specific ornithosis antigen. This is a courageous statement, one might almost call it foolhardy. Leaving aside all question of evidence for or against the possession of specific antigens by these agents, would it not be just a little odd if viruses as distinct from one another as trachoma, lymphogranuloma venereum and psittacosis were not distinguished by the possession of specific antigens? R. FAGAN (pp. 111–116) writes on *Direct Comparison of Chick Embryo and Mouse in the Isolation of the Psittacosis Agent*. In 329 attempts, 29 were successful with yolk sac inoculation of 6–8-day-old embryos or intracerebral inoculation of 3–6-week-old mice, but only 19 attempts were successful when mice were inoculated intraperitoneally.

With the established efficacy of the tetracycline antibiotics against these viruses and the knowledge that man derives infection from avian sources—parakeets and turkeys in America—it is hardly surprising that a session of the symposium should have been devoted to the control of infection in these birds by antibiotics. And the surprising thing is their efficacy; all 3 communications in Part III produce evidence that the tetracyclines adequately used can eliminate infection. K. F. Meyer and colleagues in *Chemotherapy in the Control of Psittacosis in Parakeets* (pp. 163–96) discuss the different methods of administration and the results obtained; they favour oral administration in medicated feed. R. H. BUSSELL and M. POLLARD, *Treatment of Psittacosis-Infected Parakeets with Chlortetracycline* (pp. 197–203) discuss the efficacy of this drug given intramuscularly in sesame oil, 2 doses of 5 mgm. at 3 days' interval. The results were eminently good though this method has the disadvantages of

having to handle infected birds and of producing some muscle necrosis. In the third paper: *Turkey Ornithosis Prophylaxis Using Chlortetracycline* (pp. 206–17) the authors, D. E. Davis and J. P. Delaplane, give their findings with medicated feed. 100 gm. per ton effectively prevented disease—the infecting dose gave roughly an 80% mortality—while a larger dose of 400 gm. prevented both symptoms and lesions.

The concluding Part IV consists of 2 papers one on *Federal Developments in Psittacosis Control* (pp. 221–47) contributed by J. M. ANDREWS, Assistant Surgeon General of the U.S. Public Health Service, and a short concluding one by M. Pollard on *Current Trends in Psittacosis* (pp. 248–54). *S. Bedson*

KONRÁD, J. & STRAUSS, J. Klinika, therapie a prevence ornithosy. **[Clinical Aspects, Therapy and Prevention of Ornithosis]** *Časopis Lékařů Českých.* Prague. 1958, Nov. 14, v. 97, No. 46, 1440–44, 2 figs. & 2 graphs. [21 refs.] English summary.

Between 1951 and 1955, 46 male and 4 female employees of poultry processing factories were admitted to hospital in Turnov, Czechoslovakia, suffering from ornithosis. The infection was probably acquired by inhaling dust from the feathers of infected ducks. The incubation period was 7–9 days. The onset was acute with intermittent fever, muscle pains, nausea, vomiting and headache, followed by a dry irritating cough. Radiography of the chest showed centrally situated areas of infiltration which extended later to the periphery. 3 patients developed myocarditis. Attempts to isolate a virus were unsuccessful, and the diagnosis was established by complement-fixation tests. 2 case histories are given in detail. *D. J. Bauer*

POLLARD, M. **Therapy of Psittacosis-Infected Parakeets with Chlortetracycline.** *Antibiotics & Chemotherapy.* New York. 1959, Jan., v. 9, No. 1, 23–6. [15 refs.]

Chlortetracycline in an emulsion made with sesame oil was effective in clearing parakeets of psittacosis when injected intramuscularly in a single dose of 20 mgm. Psittacosis virus was tested for by inoculating Swiss mice intracerebrally (0·03 ml.) and intraperitoneally (0·2 ml.) with a 10% W/V suspension made from spleen, liver and kidney. Passage was made with a spleen/liver suspension from mice remaining well for 14 days and birds were considered free of infection if 3 mouse passages failed to detect it. Virus was not recovered from any of 51 parakeets given 20 mgm. chlortetracycline, but was isolated from 25 of 43 untreated controls. *S. P. Bedson*

SMORODINTSEV, A. A., CHUDAKOV, V. G. & CHURILOV, A. V. **Haemorrhagic Nephroso-Nephritis.** [Translated from Russian by Catherine MATHEWS, M.Sc.] 124 pp., 13 figs. [8 (5 coloured) on 8 pls.] 1959. New York. Paris. Los Angeles. London: Pergamon Press Ltd., 4 & 5 Fitzroy Square, W.1. [60s.]

This is a comprehensive account of a disease apparently confined to Russia, Manchuria and North Korea, about which little is known to workers elsewhere in the world. The aetiological diagnosis of this condition is, however, so difficult that the disease may be more widespread than is at present thought. Published work has hitherto been entirely in Russian and largely in textbooks and lesser known journals. This review is therefore welcome and is well presented although as the latest reference cited is dated 1952, it is not up to date and must be a translation of an edition published several years previously. The date of publication of the original is not given.

The reservoir of the disease is apparently mainly the vole *Arvicola* and may be transmitted to man by contamination of skin lesions with rodent urine [see LEBEDEV, below]. Ectoparasites may or may not be involved. Human cases occur between April and November with the peak of maximum incidence earlier in the south than farther north.

As the responsible virus is not pathogenic for the usual laboratory animals no progress was made in its study until a species of vole was found to suffer a benign illness with splenomegaly and haemorrhages. Cats were then found to have fatal infections. The virus was also shown to multiply in chick embryos.

The clinical picture at onset is of fever, toxaemia, headache and sometimes vomiting. There is congestion of the face, chest and conjunctivae and epistaxis may occur. Lumbar and abdominal pain appears about the 3rd day associated with severer vomiting and hiccough. A petechial rash is found on the thorax and axillae, and haemorrhagic symptoms are common. Oliguria, albuminuria and cylindruria are associated with uraemia. About 5–7 days after onset the patient becomes afebrile but renal and haemorrhagic symptoms remain severe. Polyuria follows and convalescence may be protracted. The mortality is 3–5%.

The basic pathology is of focal vascular lesions in all organs but notably the kidneys where acute interstitial nephritis is followed by haemorrhagic nephritis due to destructive necrobiotic vascular lesions. It has been suggested that the primary lesion may be in the autonomic nervous system.

In diagnosis the condition must be differentiated from a variety of febrile haemorrhagic diseases. The differences from the principal of these are tabulated in detail. The differentiation from the other Russian haemorrhagic fevers about which little is known in the West—Crimean, Omsk and Uzbekistan haemorrhagic fevers—is particularly interesting. The resemblance of the epidemiology of haemorrhagic nephroso-nephritis to that of leptospirosis is very striking—leptospires were, however, excluded as the cause.

C. E. Gordon Smith

LEBEDEV, A. D. **Results of Expedition Study of Haemorrhagic Nephroso-Nephritis in the Yaroslavl Oblast.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1645–54, 2 figs. [27 refs.] [Translated from Russian.]

A haemorrhagic fever with associated renal disease was recognized in the Yaroslavl Oblast in European Russia in 1949–50. The annual incidence has varied

being highest in 1948–9 and 1953–4, and lowest in 1950–1, and 1955–6. Cases occur throughout the year but more than 80% of them in November–December and there were no cases in July–August. In over 80% of the houses where cases occurred there was only 1 case. The incidence was low under 7 years of age and twice as high in small villages (up to 40 inhabitants) as in large ones. There appears to be a higher incidence in workers concerned in grain purchase, flax-spinning and cattle breeding.

The chick-cell haemolysis reaction (Avakian) [not described] was positive in 60% of sera from an area where cases occurred every year but in only 10% from a nearby area less affected. 32% of sera from persons who had had the disease were positive.

The physical characters of the affected area suggest that there is a relation between clay soils and higher incidence. 11 species of murine rodent and 5 species of insectivore occur in the area. These animals invade houses in large numbers especially in September–October, more so in small villages than large ones. The only possible arthropod vectors in the area are gamasid and trombiculid mites but the former are most numerous in the spring when cases are few, the latter are confined largely to the forest and cases are commonly in persons who have no possible contact with it. The low incidence of familial spread is against the theory of respiratory or alimentary spread in man.

The hypothesis which seems to fit the facts best is that the disease is transmitted to man from the excreta of small wild animals—hence the greater incidence in persons handling contaminated materials like grain, flax and fodder, and the peak of incidence which follows the invasion of houses by animals in the autumn. Rodent extermination is said to have had excellent effects in controlling the disease.

[See this *Bulletin*, 1942, v. 17, 106, and SMORODINTSEV *et al.*, above.] *C. E. Gordon Smith*

Rheumatic Diseases

MUIR, G. S. **Rheumatic Heart Disease in Singapore. A Survey of the Morbid Anatomical Features.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1958, Sept., v. 52, No. 5, 446–53, 2 figs. [22 refs.]

The author has examined the autopsy records of 157 persons dying of rheumatic heart disease among 12,406 routine autopsy examinations in Singapore. Though the climate is warm, moist and equable, severe overcrowding in the city facilitates the spread of streptococcal infections among the population, which is predominantly Chinese.

There was a relatively greater proportion of females to males among those dying from rheumatic carditis, though twice as many autopsies were performed on males as on females. Of the 157 rheumatic deaths, 82 (19·5%) were female, 75 (9·1%) male. Moreover, though deaths in males from this cause showed a high incidence only in the 10–20 age-group, in women this was a common cause of death at all ages from 10 to 40 years.

The pericardium was affected in 65 out of 157 cases, a fibrinous pericarditis being found in 12%, an effusion in 22% and both changes in 4%. Neither of the 2 patients with adherent pericardium showed evidence of constriction. Rheumatic endocarditis affected the mitral valve only in 41% of cases, both mitral and aortic valves in 40% and the aortic valve only in 5% The tricuspid valve was involved together with other valves in 16%, and in 2% of patients all 4 valves were affected. The mitral valve showed pure stenosis in 31% of the 157 bodies, and pure incompetence in 6%. Pure stenosis of the aortic valve was noted in 15% and pure incompetence in 3%. The former figure is unusually high. Vegetations had developed on the mitral valve of 31% of the victims of rheumatic heart disease, and on 19% of their aortic valves, while in 8% both valves were thus affected.

Chronic venous congestion of the liver was found in 20% of cases, and was associated with brown induration of the lungs in 15%. Infarcts were noted in the viscera of 18% of the bodies.

Though a comparison with the incidence of rheumatic carditis noted in large series of autopsies carried out in Ceylon, Spain, Central America and the United States suggests that the disease is of less importance in Singapore than elsewhere, save in Ceylon, nevertheless it clearly constitutes a serious health hazard and one which may well increase as overcrowding becomes more intense. *J. H. Walters*

SMYTH, C. J., BUNIM, J. J., CLARK, W. S., CRAIN, D. C., DEMARTINI, F. E., DUFF, I. F., ENGLEMAN, E. P., GRAHAM, D. C., MONTGOMERY, M. M., NORCROSS, B. M., POLLEY, H. F., ROPES, Marian W. & ROSENBERG, E. F. **Rheumatism and Arthritis: Review of American and English Literature of Recent Years (Twelfth Rheumatism Review). Parts I & II.** *Ann. Intern. Med.* 1959, Feb. & Mar., v. 50, Nos. 2 & 3, 366–494; 633–787. [2323 refs.]

Heart Disease

MORTON, W., BEAVER, Margaret E. N. & ARNOLD, R. C. **Heart Disease Screening in Elementary School Children.** *J. Amer. Med. Ass.* 1959, Mar. 14, v. 169, No. 11, 1163–8.

"This report is the first of three which will deal with different facets of the entire problem of mass screening for heart disease in children. This paper deals primarily with the results of a screening program in one community and its environs."

The primary screening procedure was carried out on 6,311 elementary schoolchildren of age 5 to 14+ years in Mesa County schools, Colorado. It comprised a physical examination (which is described) and blood pressure recordings, and "in addition, lead V_3R electrocardiographic tracings and 70-mm. chest x-rays were obtained from about two-thirds of the children." A secondary screening procedure was carried out by a paediatric cardiologist on all children "who were thought to have heart disease or to need further evaluation to rule out the presence of heart disease." The findings are described with a table which sets out a comparison of age and sex with diagnostic categories. Among the 6,311 children a total of 41 cases of heart disease—33 congenital, 7 rheumatic and 1 "other"—were discovered and the majority of these were previously unknown. In addition to these cases 3 of ECG abnormality were found and in 50 children a history of rheumatic fever was obtained but the reliability of these histories could not be checked. The clinical nature of the discovered cases of heart disease is described.

"Functional or innocent heart murmurs in children are a fascinating topic" which is discussed at some length. A table sets out the frequency of these innocent murmurs and their location by age and sex in 6,269 children, in 2,068 of whom these murmurs were discovered.

There is a good discussion of the results and value of the investigation, which not only brought to light previously unknown heart disease but also showed "that there were at least 15 children who were relieved of a false diagnosis of heart disease." *M. E. Delafield*

MORTON, W., HOFFMAN, M. S., CLEERE, R. L. & DODGE, H. J. **Comparison of Three Methods of screening for Pediatric Heart Disease.** *J. Amer. Med. Ass.* 1959, Mar. 14, v. 169, No. 11, 1169–72.

"There is a need for more information regarding the sensitivity, specificity, and reliability of the various methods which might be used singly or in combination in screening for pediatric heart disease." In this paper there is presented information obtained in the examination of 5,654 schoolchildren in Colorado, each one of whom was subjected to 3 screening methods. These 3 methods comprised: (1) physical examination, with blood pressure recordings when indicated, by selected physicians experienced in cardiac diagnosis, (2) single V_3R lead of the electrocardiogram and (3) 70-mm. chest X-ray.

These screening methods led to the discovery among those 5,654 children of 36 with congenital heart disease, 5 with rheumatic heart disease, 1 with cor pulmonale and 3 with electrocardiographic abnormality. The findings are described and discussed with tables that give the age and sex distribution of the children, a comparison of the diagnostic categories with results of the 3 screening methods and a comparison of the 3 methods in respect of specificity, sensitivity and efficiency. Each method gave a certain number of both false-positive and of false-negative results.

Specificity is expressed as the ratio of true positive tests to total positive tests, sensitivity as the ratio of true positive tests to the total number of subjects with the condition for which the test is done, and the efficiency index is the product of these 2 ratios.

The general conclusion is that physical examination was both the most specific and the most sensitive method. After a careful discussion of the 3 methods mention is made of the development of the phonocardiogram which records heart sounds on hi-fi tape. This device can be operated by a technician and has various advantages such as the saving of physicians' time but "overenthusiasm for a new tool" should be guarded against. *M. E. Delafield*

See also p. 631. MUIR, **Rheumatic Heart Disease in Singapore. A Survey of the Morbid Anatomical Features.**

Cancer

NAU, C. A., NEAL, J. & STEMBRIDGE, V. **A Study of the Physiological Effects of Carbon Black. II. Skin Contact.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 511–20, 1 fig. [17 refs.]

Several different carbon blacks prepared by different methods and by different companies were tested for their carcinogenic effect by skin painting on mice, rabbits and monkeys. A few tumours appeared among 180 mice painted with one particular product; but these tumours occurred in the stomach (2), colon (1) and in the lymphatic glands and spleen (3) and not on the skin. The painting of black that had been extracted with benzene was followed by the appearance of 2

tumours in 130 mice (2 lymphosarcomas of lymph glands) and 1 sarcoma of chest wall in a single monkey painted. In contrast, benzene extracts of several types of black led to the development of skin tumours within one year in a high proportion of animals (between 33% and 85%; 3 : 4-benzpyrene was identified as one constituent of the extracts. Known carcinogens that had been adsorbed on to carbon black produced only very few tumours. It was concluded that carbon blacks as manufactured (1) produced no observable harmful effects after skin contact, (2) have absorbed a component which, when free, can produce skin cancer in mice, and (3) can effectively adsorb known carcinogens such as methylaholanthrene and 3 : 4-benzpyrene.

[It is unfortunate that Tables 2 and 7, showing details of some of the principal results, have been omitted from the printed text.] *Richard Doll*

POLHEMUS, D. W. & KOCH, R. **Leukemia and Medical Radiation.** Pediatrics. Springfield, Ill. 1959, Mar., v. 23, No. 3, 453–61. [24 refs.]

The radiation histories of a group of children who had suffered from leukaemia were compared with the histories of a control group of children who had attended the same hospital. The control children consisted mainly of consecutive surgical patients with non-orthopaedic conditions; patients whose surgical condition in itself required preceding roentgenographic studies of X-ray treatment were eliminated and a few "randomly sampled" healthy private patients were included so as to balance the number of private patients in the leukaemia group. The control children were selected (1) to match the leukaemic children in respect of their year of birth and (2) to be resident in the one county in which nearly all the leukaemic children had resided. The histories were obtained by sending questionnaires to the families of the patients. Questionnaires were sent to the families of 317 leukaemic children and satisfactory data were obtained from 251. For the purpose of comparison with the leukaemic children, only that part of the radiation history of the control children was considered which fell into the period of life which corresponded to the life of the leukaemic children before their disease was diagnosed.

The results showed that a significantly higher proportion of the leukaemic children than of the controls had been given previous deep X-ray therapy (14 : 2); in most cases the treatment had been given at birth for an enlarged thymus (11 : 2). The proportion of children who had been examined fluoroscopically was also somewhat higher in the study group (17 : 8). Similar, but less marked, differences were found in the frequency of exposure to diagnostic irradiation (pre-natal or post-natal 135 : 104; pre-natal 72 : 58). A substantial difference was also recorded in the proportion of families reporting that the children had been exposed to radiation while shoe-fitting (98 : 47), but, in this case, it was thought that "the data could not be properly interpreted because of the extreme variability of exposure".

[It is difficult to assess the meaning of these results, as the families of dead children may have tended to respond to the questionnaire more readily than the families of living children—particularly if the children had been irradiated.] *Richard Doll*

Dental Hygiene

JENKINS, G. N., FORSTER, Margaret G., SPEIRS, R. L. & KLEINBERG, I. **The Influence of the Refinement of Carbohydrates on their Cariogenicity. *In vitro* Experiments on White and Brown Flour.** *Brit. Dental J.* 1959, Mar. 17, v. 106, No. 6, 195–208. [36 refs.]

Experiments carried out by the authors showed that, when ground dental tissues or calcium phosphate were incubated in flour-saliva mixtures, only about two-thirds as much material dissolved with brown flour compared with white flour. This lowering of the solubility of calcium phosphate by brown flour was produced neither by influencing salivary acid production or *p*H changes, nor by buffering mechanisms, nor by the release of calcium and phosphate ions.

When whole teeth with waxed roots were incubated with saliva and either of the 2 flours, no differences between the amounts of enamel dissolving were consistently observed either by chemical analysis of the saliva or by visual inspection of the teeth. When part of the outer enamel was ground away, groups of teeth incubated with brown flour showed visually less evidence of decalcification in the ground areas of the enamel, but differences in the amount of calcium and phosphate dissolving were not detectable chemically.

The active substance(s) can be extracted with water from brown flour or brown bread, and such extracts can be shown to lower the solubility of whole teeth as well as of powdered materials. It is suggested that the effect of brown flour may be at least partly accounted for by the contained phytate and other organic phosphates. *Robert Weaver*

WHEATCROFT, M. G. & KLIMT, C. R. **A Survey of Oral Health, Qalyub Project, Egypt.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 1, 133–48, 7 figs.

This survey was made in 3 villages near Cairo—Qalyub el Mahatta, Mit Halfa and Qaranfil. The total

number of persons examined was 4,324, representing a 1-in-3 sampling of the populations of the 3 villages. The average number of decayed, missing and filled permanent teeth was 5·8 per person. The incidence of periodontal disease was high; it affected 45·6% of those examined. The incidence of malocclusion was low.

Of the persons examined 69% were classed as having good oral hygiene and, since none of them reported that they brushed their teeth, it was concluded that the maintenance of a clean mouth was dependent on mechanical self-cleansing factors, such as type of dental arch, tooth form and type of food consumed.

[The findings regarding caries of the deciduous teeth are puzzling. The number of persons with deciduous teeth is given as 1,696, and the number of deciduous teeth examined is stated to be 82,285—an average of nearly 49 deciduous teeth per person.]

Robert Weaver

LEWIS, F. D., Jr. & LEATHERWOOD, E. C., Jr. **Effect of Natural Fluorides on Caries Incidence in Three Georgia Cities.** *Pub. Health Rep.* Wash. 1959, Feb., v. 74, No. 2, 127–31, 1 chart.

A dental survey of 9,301 school children, aged 6–15 years, was carried out in the 3 Georgia communities of Moultrie, Savannah and Macon. The natural fluoride concentration in the drinking water of these towns was approximately 0·75 p.p.m. for Moultrie, 0·38 p.p.m. for Savannah and 0·11 p.p.m. for Macon.

The decayed, missing and filled (DMF) rate for permanent teeth per child was 1·82 in Moultrie, 2·99 in Savannah and 4·64 in Macon. Moultrie had about twice as many caries-free children as Savannah and more than 2½ times as many as Macon. These findings show that there is an inverse relationship between the caries attack rates and the fluoride concentration in the water system of the communities. *Robert Weaver*

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order: General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology

MINISTRY OF LABOUR & NATIONAL SERVICE. **The Length of Working Life of Males in Great Britain.** *Studies in Official Statistics: No. 4.* 24 pp., 3 charts. 1959. London: H.M. Stationery Office. [3s. 6d.]

A table has been constructed on similar lines to a life table based on the working life of males in 1955. The expectation of life in 1955 of males aged 15 years was 54·9 years and the expected working life was 48·4 years. The difference of 6½ years between the expectation of life and the expectation of working life was practically constant until age 60, it then increased slightly and decreased after the age of 67. The losses from the working population of young adults were almost solely due to death. Losses from the working population due to causes other than death were constant between the ages of 28–52 at 1 per 1,000 while losses from death increased from 1·3 at age 28 to 10·4 at age 52. Loss from death rose steadily to 36·9 per 1,000 at age 65 and loss from other causes rose to 28·2 at age 64 and rose to 441·2 per 1,000 at age 65. This rise was due to "retirement" under the National Insurance Act of 1948. In 1931 the loss due to other causes than death at age 65 was 107·7 and the expectation of working life was 6·4 years compared with 4·3 in 1955. The expectation of life was 11·3 years in 1931 and 11·9 in 1955.

The methods used in constructing the table of working life are given in detail. *W. J. Martin*

BROWN, H. M. & WILSON, R. N. **Chronic Bronchitis in Industry. An Account of a Trial of *H. influenzae* Vaccine.** *Brit. Med. J.* 1959, Jan. 31, 263–7. [18 refs.]

Workers in a large ironworks who suffered from bronchitis each winter were asked early in the winter of 1957 to volunteer for a course of treatment to reduce incapacity from the disease. Sufferers from chronic bronchitis among the volunteers were diagnosed by history, X-ray and lung-function tests, and the proven cases were allocated to 1 of 2 groups. Because skin tests for hypersensitivity to *Haemophilus influenzae* were positive in 63% of the bronchitic workers, a group of 151 were given *H. influenzae* vaccine in an attempt to lower morbidity by desensitizing them to this organism. A control group of 138 were given tablets of aneurine hydrochloride. The vaccine, containing 10^9 bacteria per ml., was given by injection in doses of 0·2, 0·4, 0·6 and 1 ml. twice weekly followed by 1 ml. monthly from December 1957 until March 1958.

A similar proportion of men in each group thought that their treatment had reduced the amount of illness they had over the winter. The amount of absence from work through illness was the same in both

groups. The authors conclude, therefore, that *H. influenzae* vaccine does not reduce the incidence of relapses of chronic bronchitis. *I. B. R. Duncan*

DESOILLE, H., MOLLARET, P. & KOLOCHINE-ERBER. Sur l'indemnisation des leptospiroses d'origine professionnelle. [**Compensation for Leptospirosis of Occupational Origin**] *Arch. Malad. Professionnelles.* Paris. 1959, Mar.–Apr., v. 20, No. 2, 149–51.

The main purpose of this paper is to stress that the law on industrial compensation for leptospirosis is circumscribed and out of date in that it is not in accord with the present knowledge of the different kinds of leptospiroses which may exist in man through transmission from a variety of animal reservoirs.

The views of the authors of this paper are based on the case of a young swineherd who was away from work for a month with an illness diagnosed by his doctor as swineherd fever presumably due to *Leptospira pomona.* Compensation for this illness was refused on the ground that the law which admits this infection in swineherds also prescribes that the diagnosis is not to be accepted unless serological examination yields a positive result at a titre of over 1 in 1,000. Serological tests had not been carried out at the time but were done about 8 months later The results of these tests which were carried out with 7 different leptospires were negative against all except *L. icterohaemorragiae* with which a weak positive was obtained. It is considered in retrospect to be probable that this organism was the actual cause of the illness but compensation could not be awarded because the law does not recognize that the infection may result from the work of a swineherd.

Some suggestions are made for the improvement of the existing law. *M. E. Delafield*

ASK-UPMARK, E. **How did They Die? A Study on the Occupational Mortality in Three Swedish Professions.** *Acta Med. Scandinavica.* 1959, Feb. 25, v. 163, No. 2, 89–104, 9 figs. [19 refs.]

After allowing for the variables stressed by the author in this occupational mortality survey, he concludes that 382 Swedish university men (352 professors) died from essentially the same causes as did the average man. He knew them all. He found no evidence that scholarly work favours the development of cerebral disease. These university men (group A), of whom 75% were from Upsala and Lund, died between 1900 and 1957. His other groups (B and C) were 508 Stockholm printing workers who died between 1925 and 1955, with 6 years excluded because death certificates were not available, and 741 Stockholm street-car employees who died between 1944 and 1956. In the *J. Amer. Med. Ass.* he found his control group (D), 700 American doctors who died in 1957. All were men aged 30 or over. The average age at death was: A, 68 10/12 years (range 34–94); B, 58 3/12 (30–90); C, 61 7/12 (31–93); D, 67 3/12 (34–100). The numbers living beyond 65, A's retirement age, were 250, 165, 248 and 443.

In Sweden in 1952, 68,270 men and women died; deaths from senility (3,800), ill-defined causes (1,109) and in the first year of life (1,367) were excluded; among the remainder the 9 most common causes were distributed in the categories shown in the table below. Among the 4 groups the number of deaths in each of these categories is shown in the table:

Group		A	B	C	D	Addendum
	Sweden	University	Printing	Street-car	American doctors	Printing*
Number	68,270	382	508	741	700	222
Cardiovascular	23,037	151	177	271	369	87
Cerebrovascular	9,603	53	45	103	108	22
Malignant tumour	12,085	53	97	141	108	56
bronchial		2	17	18	17	16
leukaemia		4	6	7	7	2
intracranial		4	3	21	4	–
Violence	4,047	14	30	54	24	17†
Respiratory	3,241	34	23	53	28	14
Digestive system	2,811	15	31	44	19	9
Urinary	1,769	22	20	35	29	10
Tuberculosis	1,233	5	53	25	0	3
Diabetes	851	6	5	0	6	0

[*years 1956 and 1957. †4 suicides.]

The variables in time affect the proportion of tuberculosis and of bronchial carcinoma and coronary disease. In the university men 2 of 3 cardiovascular deaths could be presumed to be from coronary disorders, and in the American doctors, 3 of 4. No radiologist died from leukaemia in Sweden or America, and no suicides were reported among the American doctors. In the Swedish groups among the deaths from violence there were 5, 17 and 28 suicides.

M. Patricia Fitzsimons

INDIA, GOVERNMENT OF: (A report from the Office of Chief Adviser Factories, Ministry of Labour). **Silicosis in Metal Grinding (Scissors and Razor Grinders in Meerut).** *Indian J. Indust. Med.* 1956, Dec., v. 2, No. 2, 6–15, 3 pls. [22 refs.]

GUPTA, M. N. **Silicosis amongst Hand-Drillers in Mica Mining in Bihar.** *Indian J. Indust. Med.* 1957, Dec., v. 3, No. 2, 8–14, 2 pls.

STÖBER, W. & BAUER, G. Zur Wertung der derzeitigen Kausaltheorien über die Silikoseentstehung. [**An Evaluation of Current Theories of the Cause of Silicosis**] *Staub.* Düsseldorf. 1959, Jan. 1, v. 19, No. 1, 1–5. [23 refs.]

This paper is introduced by K. THOMAS who states that it is concerned with the fundamental question: how do solid particles of SiO_2 exert their harmful influence upon cells? The authors classify existing physico-chemical speculations under the headings "Solubility theory" and "Surface theory"; the latter is subdivided into the matrix and contact theories.

It is considered that to accept a mechanism involving solution would be to assume (i) that monosilicic acid is the active agent, and (ii) that some of the cell walls are impermeable to dissolved silica. If either of these points can be refuted the theory will have to be abandoned.

The matrix theory necessitates the proposals that (i) only crystalline dusts cause silicosis, (ii) protein chains match the crystal lattice dimensionally and adsorb to form a surface covering, and (iii) this sheath of protein is released and commences a fibrogenic process. Against this is the fact that the substances isomorphous with silica do not cause the disease.

The essential points in contact theory are (i) that SiO_2, or some substance with similar catalytic properties, is the active agent, and (ii) that the oxygen surface atoms form a catalytic contact with the tissue which in some way produces the fibrous growth. This concept demands no special geometrical configuration and seems to fit existing experimental data satisfactorily.

C. N. Davies

MIYAHARA, K. **[A Study of the Changes occurring in the Blood and other Tissues in Experimental Silicosis, a Condition caused by Coal Dust inhaled]** *Igaku Kenkyu.* Fukuoka. 1959, Jan., v. 29, No. 1, 20–38, 10 charts & 4 figs. [29 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"Silicosis has been studied from various angles, but coal as its causal agent has seldom been experimentally investigated. The author kept rabbits in the coal dust and examined the changes produced in the lungs and in the blood.

Method and Result

"1. The coal particles given for inhalation contained 76.04% of its weight of SiO_2, and 50 to 60% of these were 5μ or less across. The air in the apparatus had 1,850–2,500 coal particles per cc. floating in it.

"2. The animals were kept in the dust for some 3 hours a day and for 1,225 to 1,284 hours in all; the experiment was continued for 515 to 554 days in some cases.

"3. The lungs were found affected in all cases, with silicotic tubercles of the size of a pin point or a millet formed by predilection in the dorsolateral surface of the lower lobe, in the marginal part of each lobe and in the subpleural portions; these were also found in the bronchus, the perivascular tissues, the subpleural areas, and the alveolar walls, with silicic dust deposited in the interstitial tissue.

"4. Blood tests: a decrease in the number of erythrocytes and a smaller decrease in the amount of hemoglobin; no appreciable change in the color index; a decrease in the number of leukocytes, a decrease in percentage and in absolute number in that of pseudoeosinophile leukocytes; an increase in percentage, but little or no decrease in absolute number, in that of lymphocytes.

"It was seen that the decrease in the number of leukocytes mainly implied a decrease in that of pseudoeosinophile leukocytes.

"These hemographic changes appeared not to aggravate beyond certain limits and the fact that there was no further hemographical improvement in animals kept out of SiO_2-containing air indicated probably that the blood-forming organs were all damaged."

DATE, O. **[On the Antibody produced by Intravenous Injection of the Rock Crystal Suspension coated with Rabbit Serum Protein and the Non-Coated Rock Crystal Suspension]** *Igaku Kenkyu.* Fukuoka. 1958, Dec., v. 28, No. 12, 4803–12, 2 figs. [22 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"The author came to the following conclusions after injecting the rock crystal suspension coated with rabbit serum and the non-coated rock crystal suspension in the rabbit's ear vein.

"1. By the intravenous injection of the rock crystal suspension coated with rabbit serum and the rock crystal suspension the author has found in the serum of injected rabbits that a certain substance agglutinates the rock crystal particles coated with rabbit serum; and that it is agglutinin.

"2. This antibody agglutinates the rock crystal suspension coated with rabbit, horse, bovine, pig, human, dog, goat, and chicken serum.

"3. This antibody is absorbed completely by the rock crystal particles coated with sera proteins of the above-mentioned kinds of animals.

"4. Thus I assume that the protein denatures after being absorbed by the rock crystal, but it is difficult to explain the mechanism of this denaturation by the solubility theory. However this mechanism can be explained by the theory of Jaeger-Seifert."

KASHIMURA, M. **[A Study of the Antibody produced after Intravenous Administration of Particulate Silicic Stone in Suspension]** *Igaku Kenkyu.* Fukuoka. 1958, Dec., v. 28, No. 12, 4813–24, 5 figs. [15 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"The silicic stone used were of four kinds, each obtainable in Japan. These were injected in suspension into the ear vein in rabbits to see whether or not each kind of silicic stone injected produced an antibody specific to it, and if so, whether or no there was any mutual relation between one kind of antibody and another and how each antibody was produced and how it disappeared.

"1. Each kind of silicic stone in particles held in suspension, when given intravenously in rabbits, produced two kinds of antibody in these animals, each capable of agglutinating particulate silicic stone coated with serum protein.

"2. One kind of antibody produced by one kind of silicic stone reacted to the other three kinds of silicic stone coated with serum protein and the other only to

the particular kind of silicic stone by which it had been produced.

"3. The protein adsorbed onto the surface of each particle of silicic stone became denatured in part and divided into three layers, one lowermost and specifically denatured, one uppermost and not denatured, and one intermediate and nonspecifically denatured.

"4. The specific antibody appeared later and disappeared sooner than the nonspecific."

OYANGUREN, H., SCHÜLER, P., MATURANA, V., GUIJÓN, C., CRUZ, E., VALENZUELA, A. & GUZMÁN, Adriana. Pesquisa radiologica de la silicosis por medio del Abreu 70mm. [**The Radiological Investigation of Silicosis by means of 70mm. Film**] *Rev. Servicio Nacional de Salud.* Santiago. 1957, June, v. 2, No. 2, 185–200.

In 1956–7 a semi-portable mass radiography unit with the 70mm. film was used to obtain information on the incidence of suspected or confirmed silicosis and pulmonary tuberculosis in workers in the coal and calcite mines and the cement and ceramic industries. The films were read by 3 doctors separately or in conjunction where there was initial disagreement. 9,984 films were examined; 6,933 from coal-miners; 606 from calcite miners; 1,359 from ceramic workers; and 1,086 from cement workers.

The results are best given in the following table:—

	coal	ceramic	cement	calcite
silicosis				
suspected	553	202	89	39
confirmed	126	37	7	11
+tuberculosis	41	14	0	1

The age-groups 45 to 55 + showed the highest incidence of both suspected and confirmed silicosis, the ceramic industry showed lung changes earlier than any other but there was a sudden large increase in the small group of calcite miners aged 55 +. 6 out of 1,283 coal-miners and 3 out of 453 ceramic workers showed evidence in less than 10 years while all in the latter industry and the calcite miners who showed evidence of silicosis had done so within 30 years.

412 patients positive to the 70mm. film were then examined with the "standard" 35 × 35 cm. film. The results showed that 82% of the cases regarded as silicosis by the 70 mm. film were confirmed but only 36·6% of suspicious cases; while 13·1% of those considered to be active tuberculosis were found to be suffering from silicosis and 1·2% of those regarded as normal were silicotics. On the basis of the sample examined the authors estimate that out of the 9,984 workers the real incidence of silicosis was between 3·8% and 8·2% though it was a selected population through requests for examination or known exposure risks.

Though incipient silicosis is much less easy to diagnose than tuberculosis they consider that the miniature film is satisfactory for the diagnosis of silicosis if followed by a standard skiagram in suspected or definite cases or where tuberculosis is found; and that systematic investigation with the miniature film will detect about 80% of all cases. *W. K. Dunscombe*

CHAMPEIX, J. & ALLAUX, R. Silicoses à forme radiologique condensante d'emblée par exposition aux poussières de silice calcinée. [**Silicosis Presenting Radiologically as Massive Shadows from Exposure to Dusts of Calcined Silica (Diatomaceous earth)**] *Arch. Malad. Professionnelles.* Paris. 1958, Sept.–Oct., v. 19, No. 5, 463–6, 2 figs.

Diatomaceous earth is dried in rotating furnaces at a temperature of 400°C. and is then ground, sifted and bagged. Workmen exposed to the dusts from these operations have been found to develop silicosis after 20–25 years. Since 1949 in a works calcining diatomaceous earth at a temperature of 950–1,000°C. a greatly increased number of cases of silicosis has been observed. The authors attribute the increased risk partly to the conversion of opal, an amorphous form of silica, to crystobalibe and partly to exposure to hydrochloric acid produced during the calcining process. The characteristics of the condition are the rapid onset of bilateral, symmetrical, confluent massive shadows, on a background of reticulation which in the majority of cases appear without passing through micronodular and nodular stages and which frequently run a rapidly fatal course. *I. T. T. Higgins*

ROCHE, L., DALLOZ, C., THERASSE, F. & BRUNE. Pneumotachographie et silicose pulmonaire. [**Pneumotachography and Pulmonary Silicosis**] *Arch. Malad. Professionnelles.* Paris. 1958, Sept.–Oct., v. 19, No. 5, 453–62, 7 figs.

The authors analyse 100 pneumotachograms from a miscellaneous group of underground miners, tunnellers, ceramic and metallurgical miners, classifying them into 5 types of increasing abnormality. The inspiratory/expiratory duration and velocity both at rest and on exercise correlated with the Forced Expiratory Volume percentage but such measurements failed to separate normal from abnormal tracings because of the wide scatter of the individual readings. There was no relation between X-ray category of pneumoconiosis and the various pneumotachograph ratios investigated. The authors conclude that the pattern alone of the pneumotachogram is valuable and if this is indisputably abnormal respiratory impairment is indicated.

I. T. T. Higgins

BELLINI, F. & GHISLANDI, E. Su due casi di silicosi e sclerodermia. [**On Two Cases of Silicosis with Sclerodermia**] *Med. d. Lavoro.* 1959, Jan., v. 50, No. 1, 63–70, 4 figs. [25 refs.]

The English summary appended to the paper is as follows:—

"The presence in sclerodermic subjects of a polymorphus pulmonary fibrosis is recalled. Two cases are reported in which scleroderma appeared in silicotic subjects: the first, 33 years old, had a short but intense exposure to silica dusts and scleroderma apppeared at a young age; the second, 55 years old, worked for

a long time in a dusty trade and showed at a mature age sclerodactylia subsequently extended into scleroderma. In the first case the x-ray picture of the lungs was characterized by intense reticulation and diffuse micronodulation, parenchymatous shadows at the right basis, egg-shell calcification of lymphnodes; the second case showed areas of subpleural thickening in apico-subclavear regions, areas of emphysema in both medium pulmonary fields, thick pleural streaks in medio-basal regions. In both patients a concurrent tubercular infection was often suspected, but always found negative; in both cases the course of silicosis became worse at the same rate as the onset of scleroderma. It is suggested that the superimposition of both these diseases could lead to worse pulmonary conditions: it is recalled in this regard that similar immunological aspects were recently showed in the pathogenesis of both silicosis and scleroderma."

MAGISTRETTI, M., SARTORELLI, E. & PEIRONE, E. Studio dell'emodinamica polmonare dei silicotici mediante il cateterismo cardiaco. [**A Study of Pulmonary Haemodynamics in Silicotic Patients by means of Cardiac Catheterization**] *Med. d. Lavoro.* 1959, Jan., v. 50, No. 1, 45–56, 3 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"Pulmonary hemodynamics were studied by means of cardiac catheterization in 30 silicotic patients, grouped as follows: 10 with reticular micronodular silicosis, 5 with discrete nodular silicosis, 9 with confluent nodular silicosis and 6 with massive silicosis. Cardiac catheterization showed, in most of the examined subjects, an increase of total vascular pulmonary resistance and particularly of arteriolar pulmonary resistance. A parallel increase of mean blood pressure was observed in the pulmonary artery.

"Two main factors must be taken into account for the pathogenesis of these hemodynamic changes:

"1) decrease of capillary pulmonary bed and the arteriolar lesions (anatomic factor);

"2) the decrease of alveolar pO_2 following alveolar hypoventilation or arterial anoxemia (functional factor).

"The collected data suggest that the anatomic factor has a considerable importance in determining pulmonary hypertension in the course of silicosis, as indicated by the following facts:

"1) in more than half of the cases in which an increase of the mean pulmonary arterial pressure was observed in basal conditions, there was no arterial hypoxemia;

"2) the mean values of cardiac output, expressed as cardiac index are within normal limits in all forms of silicosis, while the mean values of pulmonary pressure and of arteriolar pulmonary resistance are above normal levels, which points to reduced elasticity of the pulmonary vascular system;

"3) only in a few cases the inhalation of pure oxygen, increasing the O_2 arterial saturation has produced a definite decrease of pulmonary hypertension down to normal or slightly above normal values;

"4) the increase of cardiac output, secondary to even light muscular work can induce a marked pulmonary hypertension, without arterial hypoxemia."

POLICARD, A. & JARRY, J. J. Sur le diagnostic anatomopathologique de la silicose et de sa complication tuberculeuse. [**On the Pathological Diagnosis of Silicosis and its Tuberculous Complication**] *Arch. Malad. Professionnelles.* Paris. 1958, Sept.–Oct. v. 19, No. 5, 482–4.

Criteria for the radiographic diagnosis of silicosis are legally fixed but there is at present no legal definition of pathological criteria. Considerable differences may therefore occur between histologists called to testify. This short paper gives the views of a group of French specialists who met to decide suitable definitions and lay down the pathological characteristics that would permit the certain diagnosis of pneumoconiosis. They do not consider their views to be in any way final since as they put it *"Rien n'est definitif dans la Science".* *I. T. T. Higgins*

MATSUOKA, M. [**Studies on Experimental Silicotuberculosis. Comparative Investigations on the Experimental Silicotuberculosis by the Amounts of Free Silicic Acid contained in Dust.**] *J. Sci. of Labour.* Tokyo. 1959, Feb., v. 35, No. 2, 112–36, 10 figs. on 2 pls. [80 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"In order to investigate the difference by the amounts of the contained free silicic acid in dust in the progress of silicotuberculosis complicating silicosis, the author performed the following experiment. Experimental animals were divided into four groups: the first group inhaled the dust containing much free silicic acid (SiO_2 91.28%) for a shorter period (about 300 times in 268–474 days), the second group inhaled the same dust for a longer period (about 500 times in 484–896 days), the third group inhaled the dust containing less free silicic acid (SiO_2 38.60%) for a shorter period, and the fourth group inhaled the same dust for a longer period. Each group was injected bovine typed tubercle bacilli intravenously, and the lesions were comparatively observed.

"1) In comparative investigation on the groups which inhaled the same dust, the tuberculous lesions were in more remarkable exacerbation in number, size and exudation in the group which inhaled the dust for the longer period.

"2) In observation on the groups which inhaled different kinds of dust for the same period, no macroscopic difference on the tuberculous lesions was observed. Histological investigation revealed, however, that the group which inhaled the dust containing more free silicic acid had slightly worse lesions.

"3) More dust cells were observed in the alveoli of the lungs of the groups which inhaled the dust longer, and the ones which inhaled the dust containing more free silicic acid, and they were supposed to be related to the exacerbation of the tuberculous lesions.

"4) No exacerbation of silicotic lesions by the coexistence of tuberculous lesions was observed."

SUTTON, D. A., MIDDLETON, M. D. & BODY, R. A. F. **Reaction of some Silicates with Chelating Agents.** *Nature.* 1959, Jan. 10, v. 183, 99–100, 1 fig. [10 refs.]

Mineral silicates have been directly implicated as fibrogenic agents in certain types of pneumoconiosis, particularly asbestosis. If silicates and quartz dissolve *in vivo*, the silicate ions released may produce precipitated silicates by reaction with body metals. The practical problem is whether the dissolution of fibrogenic silicates might be achieved *in vivo* by chelating agents according to the reaction:

silicate of metal *a* (insoluble) + chelate of metal *b* (soluble)→chelate of metal *a* (soluble) + silicate of metal *b* (soluble).

The purpose of such research is to discover any possible chemical approach to the therapy of pneumoconiosis.

In this study carried out at the South African Institute for Medical Research, Johannesburg, the silicates used were (a) olivine, crocidolite, chrysotile, talc and orthoclase from South African mines; (b) those of $Ca^{2}+$, $Mg^{2}+$, $Al^{3}+$, $Fe^{2}+$ and $Cu^{2}+$ precipitated from aqueous solutions; (c) tricalcium silicate made at 1500°C. In most of the experiments the trisodium salt of ethylene diamine tetraacetic acid (Na EDTA) at *p*H 7·4 was used as the chelating agent; penicillamine and glycine were also tried. Details of the methodology are given in the paper.

The conclusion is that ethylenediamine tetraacetic acid at body temperature reacts so slowly with the mineral silicate types studied that its therapeutic application in this respect, if any, will be restricted to a few selected cases. The research is proceeding and will be the subject of future papers by the authors.

A. Meiklejohn

HODKINSON, J. R. **German Research and Techniques in Airborne-Dust Measurement and Suppression in Coal Mines.** *Trans. Inst. Mining Engineers.* 1959, Mar., v. 118, Pt. 6, 397–409, 5 figs. [48 refs.]

The Tyndalloscope is used for the routine measurement of dust concentrations in the air of German coalmines. It is compact and easy to use. The Tyndalloscope reading is interpreted in terms of the mass concentration (mgm./m³) of dust of all sizes, although it is not claimed that this value is the true concentration since variations in size-distribution and composition cannot be taken properly into account. The physical basis of the instrument is discussed. It appears that the errors in estimation are commonly in the direction of over-estimating the dust concentrations, so that they tend towards safety.

The konimeter is used for determining the ash content of the dust. The konimeter dust spots are photographed before and after ashing, and the ash fraction is then estimated by comparing the photographs.

Routine measurements of dust concentrations (Tyndalloscope) and of ash content (konimeter) are combined to classify the dust level in a working place as low, medium, high, or very high. The routine of sampling is described. On each occasion of sampling the appropriate mean dust level is entered on each miner's record card. Periodic X-ray and medical examinations are made of all underground workers.

In Germany the use of water to suppress dust before it can become dispersed is similar to British practice. Water infusion of the coal is widely practised. All spray nozzles used for dust suppression must first have been approved for the particular purpose. Much effort is expended in removing dust that has become airborne. The mist-curtain is compulsory in hard headings. Because of its greater convenience, and in the interests of comfort, the use of dry filtration instead of the mist-curtain in headings is gaining favour. Some types of dry filter are described.

An aerosol technique which is intended not to remove dust from the air but to reduce its long-period retention in the lungs is being studied. It has been reported that when animals breathed fine quartz dust together with a fine salt aerosol the dust was deposited in the bronchioles instead of reaching the alveoli. The explanation offered is that many salt particles coagulate with each dust particle, so that on inhalation there is rapid condensation of water on the salt and the enlarged particle is therefore deposited higher in the respiratory tract. The coagulation and condensation effects have been confirmed qualitatively, and it is proposed to observe the effect of a condensation aerosol on alveolar retention in the human lung.

Thomas Bedford

SCHREIBEIS, W. J. & SCHREIBEIS, L., Jr. **Free Silica Dust Concentrations measured in Nine Brick Manufacturing Plants.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 485–8, 3 figs.

Dust concentrations were determined by midget impinger with light field illumination at 100 × magnification and counting only particles below 5 microns. The lower limit of particle size detectable with the optical system employed is not stated.

Samples for silica content were collected on filter paper; the dust was washed off with ethanol and particles below about 5 microns were siphoned off and analysed by X-ray diffraction.

The factories fell into 3 groups, 2 fireclay brick plants had dust concentrations up to 122 million particles per cu. ft., but the content of free crystalline silica was below 10%. 6 similar plants had lower dust counts but the silica was higher than in the other 2. One plant, making high-silica bricks, yielded free silica contents up to 90%.

Methods of dust control in use at the plants for the various processes are described but their effectiveness was not verified.

C. N. Davies

ASSET, Gabrielle. **Nasal Sampling of Aerosols in Experimental Animals.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 460–63.

Unpublished experiments by K. R. MAY are compared with some carried out by the author [this *Bulletin*, 1957, v. 32, 671]. In each series a sampling nozzle was made in the form of the head of a guineapig, with aspiration through the nostrils, and samples were taken from a moving stream of airborne particles.

The ratio of the concentration of particles in the sample to the concentration in the original stream of

air decreases as the particle size and the wind speed increase, but if the sampling speed is lower than the wind speed an optimum particle size may exist for which the ratio exceeds unity. Particles greater than a certain size (about 20 microns) cannot enter the nose. *C. N. Davies*

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Communication hors-série. L'étude de la ventilation des mines par l'analogie électrique [**Study of Ventilation in Mines by the Electric Analogue System**] [PATIGNY, J.]. 1958, 36 pp., 27 figs. [16 refs.] [Reprinted from *Rev. Universelle des Mines*, v. 14, No. 11.]

Adjustment of the ventilation of a mine is a difficult problem because there are so many inter-connecting pathways of air flow. The alteration of any one of them produces changes in the others which are not easy to predict. One of the most popular methods of forecasting the distribution of air flow is to employ as analogues electric currents in a circuit of wires which simulates the branching and joining airways.

This paper gives a detailed account of the theory behind the electrical analogue computer and describes a novel practical realization of the technique.

The first section describes basic hydrodynamic theory. This comprises the law of conservation of flow, Bernouilli's theorem and the law of frictional loss. Both non-compressible and compressible flows are dealt with and it is shown for each that the pressure drop between two points is proportional to the square of the flow rate.

Having set up the flow equations for a complex network of ducts the second section of the paper deals with their solution. This is only possible graphically or by successive numerical approximation, and each method is explained.

The electrical analogue system enables direct solution of the equations to be avoided but encounters the difficulty that non-ohmic resistances are required. This has been overcome in the past by using incandescent lamps since the resistance of these rises as the filaments become hotter with increasing current. In the computer which is described filament lamps have been replaced by adjustable resistances which, when handled in a certain way, enable a balance of currents to be set up which is a valid representation of the air flow.

C. N. Davies

MOLITOR, L., MOSINGER, M., BARTHEL, J., HEYART, H. & PÉRINET, G. Recherches sur les poussières de laminoir et leur capacité pathogène. Les sidéroses pulmonaires. [**Research on Dusts from Rolling Mills and their Pathogenic Effects. Pulmonary Siderosis**] Reprinted from *Bull. Soc. Sci. Méd. Luxembourg*. 1957, Aug., 127 pp., 170 figs. [36 refs.]

The term siderosis was proposed by ZENKER in 1867 for lung disease caused by inhaling dust of iron and iron oxide. An account is given of the history of the disease. Dust samples were collected in 6 rolling mills and subjected to chemical and physical analysis. Sampling was carried out at breathing level but no attention seems to have been given to the selection of respirable particles so that it is uncertain whether the material analysed was comparable with dust actually causing the disease.

The principal constituents of rolling mill dust were metallic iron and its oxides; the silica content was insufficient to cause silicosis. The dust, therefore, caused pure siderosis.

Guineapigs and rats were exposed to sieved dusts in experimental chambers for 2 or 3 hours daily. Siderotic nodules formed in their lungs by a mechanism initiated on the alveolar septa, as in silicosis, but the lesions regressed when exposure to dust ceased. Various other organs were involved in the syndrome of siderosis and it seemed that some toxic action must be attributed to the dust. *C. N. Davies*

SABNIS, C. V., BANERJI, S. K. & BANERJI, A. K. **Health Hazards in Foundry Industry.** *Indian J. Indust. Med.* 1958, Sept., v. 4, No. 1, 42–57.

COCHRANE, A. L., HIGGINS, I. T. T. & GILSON, J. C. **Yet Another Industrial Pneumoconiosis?** *Tubercle*. 1958, Dec., v. 39, No. 6, 399–400.

The Medical Research Council Pneumoconiosis Research Unit, Cardiff, carried out a medical survey among a random sample of iron and steel foundry workers between the ages of 55 and 64. The control group consisted of men who had not been exposed for more than one year to any fumes that might damage the lungs, or to any dusts thought likely to cause pneumoconiosis. The radiographs were categorized by 4 experienced readers, using the International Classification, without any knowledge of the industrial histories. Several causes of pneumoconiosis were identified among the controls and on investigation it was discovered that with one exception—a painter—all had spent a considerable time on the footplate of railway engines, either as driver or stoker.

X-ray category and ¾-second forced Expiratory volume (FEV 0·75*) of men at Staveley aged 55–64 who had worked more than 30 years on the footplate

No. of men	No. of years on footplate	X-ray category 1st reading	X-ray category 2nd reading	FEV 0·75 (litres)		Average age years	Average FEV 0·75 at this age (based on agricultural surveys)
7	30–39	0	0	3·28		56·5	2·43
		0	0	2·55			
		0	0	2·38			
		0	0	2·08	Mean 2·61		
		0	½	2·13			
		½	0	2·95			
		½	1	2·88			
10	40–49	0	0	3·20		58·4	2·35
		0	0	2·35			
		0	0	1·98			
		0	½	2·65			
		½	0	2·88	Mean 2·54		
		0	1	2·63			
		½	1	3·13			
		1	2	2·33			
		2	2	2·65			
		3	3	1·63			

*For comparison with previous publications from this unit the FEV 0·75 × 40 equals the Indirect Maximum Breathing Capacity (MBC) in litres/minute.

Category ½, it is explained, is an experimental category in which specific opacities can be seen in the chest X-ray but not to the extent required to diagnose category 1. *A. Meiklejohn*

TOLOT, F. & CZUCHRO. Fréquence comparée des manifestations saturnines chez les sujets exposés au risque. Éléments de pronostic. [**Comparative Incidence of Manifestations of Lead Poisoning in Persons at Risk. Prognostic Features**] *Arch. Malad Professionnelles.* Paris. 1958, Nov.–Dec., v. 19, No. 6, 606–11.

Recognizing the uncertainty which underlies any attempt to give a prognosis when the clinical symptoms of lead poisoning have disappeared, the authors reviewed 44 cases of confirmed occupational poisoning, examined several times since 1949. They took into account the frequency of characteristic symptoms, the pathological findings when known, their relation to the duration and date of exposure and whether exposure had been continuous or interrupted. The length of exposure varied from 1 to 50 years, with a mean of 16. 33 patients had one or several attacks of colic, generally within the first 5 years. Neuritis in 5 cases appeared 3 to 12 years after exposure (mean 8·2). In itself benign, though slow to disappear, it generally indicated a severe degree of poisoning, 3 of the patients later developing chronic hypertensive nephritis. The frequency of the latter disease was 16 in 44; the exposure varied from 6 to 34 years (mean 14·8); nearly one-half of the 28 exposed for over 10 years and nearly all the 11 exposed for 15 years were affected, and earlier all had had attacks of colic.

Among 16 persons exposed for less than 10 years there were 3 cases of renal or hypertensive disease. The mean age of those free from renal damage after 10 years of exposure was 45·7; and of those with renal damage was 45·6, and therefore presumably age in itself was not a factor. Thus the renal damage determines the prognosis, but colic was found to be the most important prognostic symptom because all who were removed from exposure after the first attack remained free from renal damage. Stippling, found only in the recent cases, though decisive in diagnosis, was of less value in prognosis, its presence only denoting current exposure. Mild or early attacks of colic should not be disregarded. Repeated attacks were not without risk to the kidney. Only twice in the 16 patients were renal or hypertensive attacks the presenting symptoms of illness: they were usually preceded by others, colic in 11, colic and neuritis in 2 and neuritis in 1. 2 prophylactic rules to keep in mind were suggested: the need to cut short bony deposition by modern methods of treatment, and the need to remove completely from exposure those subjects with prolonged blood changes and several attacks of colic.

M. Patricia Fitzsimons

BURSTIN, M. Coliques de plomb et appendicite. [**Lead Colic and Appendicitis**] *Arch. Malad. Professionnelles.* Paris. 1959, Mar.–Apr., v. 20. No. 2, 189–91.

The purpose of this short paper is to emphasize the great difficulties which may exist in the differential diagnosis between lead colic and appendicitis. References to the literature which are quoted record instances of lead colic diagnosed as appendicitis and also of grave cases of appendicitis which were not operated on in time to save life because of a wrong diagnosis of lead colic.

There is a description of the case of a young man, a worker in an accumulator factory, who was admitted to hospital with the diagnosis of possible appendicitis in a man with lead poisoning. Surgical operation was carried out but symptoms of colic did not cease until after a course of medical treatment.

The most important points on which the differential diagnosis is based are described. *M. E. Delafield*

HOLTAWAY, J. S. **Evaluation and Control of Lead Exposures in Powder Metallurgy Operations.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 481–4, 1 fig.

This paper reports a study of exposure to lead in an industrial plant engaged in the production of sintered powdered metal products. The principal raw materials used were copper, iron, lead, tin, graphite and powdered silica. The lead used was the metallic form of an extremely fine particle size and it was present in some of the powder mixes in the proportion of 3–6%. The processes included weighing, mixing and blending, followed by pressing to evolve the shapes and sizes of the finished products. The resultant pieces or "compacts" were then sintered in electric furnaces before the final operations of machining, grinding, buffing, inspecting and shipping. Machines were exhausted by local exhaust hoods connected to unit type collectors which recirculated air containing metallic lead dust of extremely small particle size. In some instances the discharge stream of the collectors from the presses contained concentrations of lead as high as 0·70 milligrammes of lead per cubic metre of air. The filters in the collectors were cleaned by manual shaking and brushing and it was necessary to empty the collectors frequently. Improper hygienic and safety practices such as dry sweeping and the indiscriminate use of air hoses to clean off machines and clothing, added their share of dust to the general pollution of the atmosphere.

Samples of urine were collected from 122 employees in order to determine urinary lead output. [It is not indicated whether the samples were 24-hour specimens or otherwise.] 14 employees had a range from 225 to 471 microgrammes of lead per litre of urine, with an average of 300 microgrammes. 19 air samples collected with electrostatic precipitators over 30-minute periods disclosed a mean of 0·26 milligrammes of lead per cubic metre of air, and a range of 0·06 to 0·90 milligrammes.

A new system of ventilation was installed which avoided recirculation, vacuum cleaning was substituted for dry cleaning, and an educational programme was introduced to secure employees' cooperation in maintaining good housekeeping and eliminating improper and unhealthy practices. One year later urine and air analyses for lead demonstrated that the hazard had been brought under control. *P. J. R. Challen*

KEPLINGER, M. L., TEBROCK, H. E. & DEICHMANN, W. B. **The Pharmacological Effects of Magnesium Arsenate Phosphor upon Experimental Animals.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 504–7, 2 figs.

Magnesium arsenate, a luminescent chemical, shows a red fluorescence when excited by ultraviolet radiation. For this reason the material has potential use as a colour correction phosphor in high-pressure mercury vapour and fluorescent lamps and as a red phosphor in fluorescent sign tube manufacture. Operations employing the material may involve dust exposures, and although chemically it is relatively insoluble it was felt that its toxicity should be evaluated.

The approximate lethal dose (ALD) was detremined by the method of DEICHMANN and LEBLANC. For magnesium arsenate phosphor the ALD is 0·28 gm./kgm. for rats (orally), 2·1 gm./kgm. for rats (intraperitoneally), 4·7 gm./kgm. for mice (orally) and 0·08 mgm./kgm. for rabbits (orally).

When the phosphor was administered orally to rats, mice and rabbits it caused marked irritation of the gastro-intestinal tract. The compound was poorly absorbed from parenteral sites of injection. Intraperitoneal injections into rats caused death, but at a dose much higher than the lethal oral dose. Subcutaneous and intramuscular injection into dogs caused local irritation and tissue damage. Repeated subacute doses (orally to rats 3 times weekly) caused loss of body weight, lymphocytopenia, neutrophilia and death. Dimercaprol (BAL) prevented death from the oral administration of this compound in rats, but not in rabbits.

Rats kept in a hot environment (36°C.) succumbed to a much smaller dose of the arsenate than those kept at room temperature. Those kept in a cold room (4°C.) withstood much larger doses.

The original should be consulted for full details concerning dosage and the pathological findings.

P. J. R. Challen

ARCH. INDUST. HEALTH. Chicago. 1959, Feb., v. 19, No. 2, 91–267, numerous figs. [Numerous refs.] **Conference on Beryllium Disease and its Control held at the Massachusetts Institute of Technology, Sept. 30–Oct. 1, 1958**

This number of the *Archives of Industrial Health* is devoted to 30 papers given at a Conference on Beryllium Disease and its Control, organized by Dr. Harriet HARDY at the Massachusetts Institute of Technology. Dr. Hardy is to be congratulated on bringing all these authors together and Professor DRINKER for publishing the proceedings. This number of the *Archives* can be likened to the Leroy GARDNER memorial book *Pneumoconiosis* which was largely devoted to papers on beryllium disease given at the sixth Saranac Symposium in 1947 [this *Bulletin*, 1948, v. 23, 520]. The first conference came at a time when the epidemic of acute beryllium disease was at its height and chronic beryllium disease was getting into its stride. There was at that time still doubt in the minds of some as to whether the disease existed as an entity at all and confusion among the rest as to the pathological mechanism of the disease and what it should be called.

During the 11 intervening years people associated with different industries in many parts of the U.S.A. have had experience in treating the disease, in preventing new cases and in experimental work with various aspects of the disease.

At the present time acute cases have ceased to occur and new chronic cases are due to exposure many years ago. Interest in the disease, however, remains for various reasons. There are about 200 persons suffering from the chronic form of the disease. The details of the pathological mechanism of the disease are still not fully known, nor is the possible relationship with sarcoidosis understood. Also, there always remains the possibility of further outbreaks of the disease in other industries using beryllium for new purposes.

In the first paper of the conference, A. R. KAUFMAN (pp. 91–93) describes some of these new uses of beryllium, and its compounds.

For the past 7 years Dr. Hardy has kept a registry of cases of beryllium disease from all parts of the U.S.A. The next 2 papers (PEYTON, M. F. & WORCESTER, J. pp. 94–99; and HALL, T. C. *et al.* pp. 100–3) present the epidemiological and clinical data derived from the 606 cases included in the registry. The difficulties of collecting epidemiological data are discussed. There has been about a 4-fold increase in the number of cases over the past 10 years. The attack rate in the exposed populations studied, for both acute and chronic beryllium disease together, over a 13–20-year period is approximately 7%. The case fatality rate for this group has varied between 6% and 23%. Despite the fact that a delay of 15 years between last exposure and onset of the disease is recorded, nearly one-half of all chronic cases developed symptoms or signs within one month of their last exposure. Though the chronic disease is predominantly respiratory, there is good evidence from the number of other body organs affected that the disease is a systemic one.

In a report of 20 chronic cases studied over 5–10 years, E. M. KLINE and T. W. MOIR (pp. 104–9) show several differences between persons exposed to 2 different types of beryllium and suggest that there are other pathogenic factors, in addition to sensitivity, which may be important.

J. M. DENARDI (pp. 110–16) gives the recent follow-up experience of his extensive series of cases drawn from beryllium extracting and beryllium-using industries and non-occupational cases. It is noteworthy that no new cases of the acute disease have occurred since 1953, but 33 new cases of the chronic disease have been diagnosed. His tables show "very evident" beneficial effects of steroid therapy. It would be helpful if more of the evidence was included, because the criteria for his clinical classification of C1–C4 are not given, nor are the methods of assessment.

Having reviewed all the X-rays of cases of chronic beryllium disease in the registry, J. E. GARY and R. SCHATZKI (pp. 117–25) suggest that the hypothesis of a progression of X-ray changes in one individual, from normal through linear fibrosis, granulation, reticulation

to nodulation, is unfounded. They consider that each individual responds in one of several ways, but does not progress from one pattern to another. They comment on 9 asymptomatic cases with X-ray findings consistent with beryllium disease. They agree with G. W. CHAMBERLIN (pp. 126–31) that a definitive diagnosis of beryllium disease cannot be made from X-rays alone, and that the X-ray appearance bears little relation to symptoms or the results of pulmonary function tests. 8 case reports are given.

There is an excellent paper by E. A. GAENSLER *et al.* (pp. 132–45) on *Respiratory Pathophysiology in Chronic Beryllium Disease.* Their data are based on the detailed study of 30 patients, some of whom were treated with corticotrophin and corticosteroids and studied over 5 years. Their patients were on the whole less severely affected than others previously reported. The relative inability of conventional ventilatory function tests compared with special carbon monoxide and oxygen diffusion studies to detect abnormalities in beryllium disease is well illustrated. The single most consistent and most significant abnormality was an elevation of the alveolar-arterial oxygen pressure difference. This was shown to be at least partly due to "lung shunt" rather than as previously claimed entirely due to an impediment of oxygen diffusion. The typical response of patients to long term steroid treatment was a temporary improvement in ventilatory capacity followed by a return to previous levels within a year. There were no long term effects on the alveolar-arterial oxygen gradient. The fact that no patients deteriorated while on treatment was thought to be due to their being mild cases in the first place (2 others not on treatment also remained static) rather than due to the treatment. The authors conclude that these studies are valuable in assessing the type and degree of pulmonary insufficiency and for the objective assessment of the effect of treatment. They are not helpful in formulating a specific pathological diagnosis. The average results of these beryllium cases were the same as those of 45 cases with sarcoidosis. B. G. FERRIS (pp. 146–9) augments these findings with a description of 4 further cases.

There are several papers on the problems of diagnosis of beryllium disease. G. H. CURTIS (pp. 150–3) reviews his experience with the patch test in cases of beryllium disease, chronic fibrosing interstitial pneumonitis, sarcoidosis and other pulmonary diseases, and concludes that the test cannot stand alone as an absolute pathognomonic sign for the presence of beryllium granulomatosis, although a positive test was obtained in all 32 cases of chronic berylliosis. In discussing this paper B. H. WAKSMAN (pp. 154–6) describes some experimental evidence on the nature of the hypersensitive state and disagrees with some of Curtis's theoretical explanations of his findings. The difference in time and degree of sensitization by soluble and insoluble beryllium salts is discussed, and the similarity of the problem to sensitization by mercury, nickel and cobalt is mentioned. The unusual length of the latent period between exposure and onset of disease, and the fact that beryllium may be present in the tissues for long periods without causing disease raise difficult problems. These problems cannot be answered without data on the state of sensitivity of these patients in the latent stage, but as skin testing with soluble beryllium salts itself produces sensitivity Waksman believes it to be a potentially dangerous procedure.

H. S. VAN ORDSTRAND (pp. 157–9) gives a brief and excellent account of the typical clinical pictures of beryllium disease, and H. L. ISRAEL and M. SONES (pp. 160–3) an account of sarcoidosis. Both agree that the majority of cases can be distinguished, but that a small minority exists in whom differential diagnosis is very difficult.

A. O. SEELER (pp. 164–8) describes the difficulties of assessing the effect of steroid therapy in his own patients and all those included in the beryllium registry. It is his impression that steroids should be used as soon as pulmonary function tests reveal a diffusion block. J. SCHUBERT and M. W. ROSENTHAL (pp. 169–78) review the mechanism by which aurintricarboxylic acid (ATA) acts as an antidote to beryllium in experimental animals. They suggest that beryllium can be inactivated without being excreted and also that ATA is not more toxic than other intravenously administered dyes.

The pathological changes in acute and chronic beryllium disease are described by J. B. HAZARD (pp 179–83) and H. R. DUDLEY (pp. 184–7) respectively and discussed by D. G. FREIMAN (pp. 188–9). The importance of the interstitial inflammatory reaction between the granulomata in chronic beryllium disease is stressed and it is suggested that this may account for the greater severity of symptoms in beryllium disease than sarcoidosis.

A. J. VORWALD and A. L. REEVES (pp. 190–9) describe the tissue response in rats subjected to intratracheal injection or inhalation of beryllium oxide or sulphate. Both inflammatory and neoplastic changes were produced. They found that beryllium in the blood is associated with the inorganic anions of the sera rather than with proteins. They also report some specific effects of beryllium compounds on various enzyme systems.

The part played by medical measures in the prevention of disease in those exposed to beryllium is described by J. F. ZIELINSKI (pp. 200–2) and discussed by H. L. HARDY (pp. 203–4). The exclusion of workers with a history of various pulmonary diseases, the importance of 14 × 17 X-ray films, the education of new employees and the unsuitability of skin tests as a screening test are mentioned.

J. CHOLAK (pp. 205–10) reviews the colorimetric, fluorimetric and spectrographic techniques of beryllium analysis and gives some data on the natural occurrence of beryllium in soil, coal, air and lungs.

There are 6 papers on various aspects of the control of beryllium disease by engineering techniques. E. C. HYATT *et al.* (pp. 211–20) describe the type of beryllium exposures and methods of control encountered in the Atomic Energy Commission's establishment at Los Alamos. H. M. DONALDSON (pp. 221–4) and A. EPSTEIN (pp. 225–30) each describe the problems encountered in large beryllium smelting works, the latter emphasizing the importance of simple safe handling techniques. R. I. CHAMBERLIN (pp. 231–8) gives an

excellent account of the control of beryllium machining operations. The special requirements of the job led to the development of a high-velocity, low-capacity ventilating system. The effectiveness of the system is shown by air-sampling results from inside and outside the laboratory.

F. J. VILES (pp. 239–53) describes the principles of volatilization and mechanical dispersion by which air becomes contaminated with beryllium. The mechanics of contaminant entrainment are given, together with examples of practical application.

L. SILVERMAN (pp. 254–62) describes possible ways of limiting the contamination of the neighbourhood of beryllium-using plants. First he shows that the ratio of the tentative maximum allowable concentrations of beryllium for outdoor and indoor exposures, which is 1 : 200, is of the same order as some other noxious agents. The extent and the character of the beryllium produced by various operations is described. He concludes that on a basis of present knowledge, it is possible to select air- and gas-cleaning equipment effective enough to obtain control to values well below the tentatively established neighbourhood limit of 0·01 μgm. per cubic metre. Such control can be obtained at reasonable costs not exceeding 5% of plant capital costs. They will be well below this value when it is realized that recovery of many effluents is necessary for reprocessing and reclaiming of materials.

The final paper by C. R. WILLIAMS (pp. 263–7) is an evaluation of the exposure data available in the beryllium registry. The uncontrolled use of beryllium and its compounds can produce a high incidence of beryllium disease and the mortality rate is high. The use of a standard of 2·0 μgm. per cubic metre has been shown to be relatively safe and is probably conservative. The evidence in the registry indicates that with lower exposures the delay in onset increases and the severity of the cases decreases. Thus many years must elapse before our present standards are demonstrated to be safe. Furthermore, it has been shown in all operations that this figure can be achieved: thus any attempt to increase the hygienic standard must be based on compelling evidence.

The report of this conference is extremely valuable to all present or potential users of beryllium, and their medical and engineering advisers. The conference did not solve the problems of the diagnosis of difficult cases or the pathological mechanism of the disease and comparatively few new ideas were put forward. However, the presentation and discussion of the experience of those most closely connected with beryllium and the disease that it may produce over 20 years are of considerable practical importance.

The history of beryllium disease reveals again that the cause of disease may be discovered by epidemiological techniques and successful methods of control can be instituted before the pathological mechanism of the disease is understood. *C. H. Wood*

GUPTA, M. N. **Hazards in the Dichromate Industry.** *Indian J. Indust. Med.* 1956, Mar., v. 1, No. 3, 12–34.

HOWARD, O. H. & WEBER, C. W. **A Portable Continuous Analyzer for Gaseous Fluorides in Industrial Environments.** *Arch. Indust. Health.* Chicago. 1959, Mar., v. 19, No. 3, 355–64, 11 figs.

BROWNING, Ethel. **An Evaluation of the Methods of Assessment of the Toxicity of Chemical Compounds.** *Trans. Ass. Indust. Med. Officers.* 1959, Jan., v. 8, No. 4, 138–43.

The difficulty is that of deciding which, if any, of the several methods of estimating toxicity is the best. Classifying them as investigations in library, laboratory or field, the results of all of which should be combined and correlated, the lecturer pointed out that identification of the actual chemical to be investigated was the first essential. This, because of mixtures of chemical compounds and their trade names, often presented difficulties; these could be overcome by subsidiary labelling of the constituents, with their proportions, or even by indicating to which group of organic chemicals they belong.

The annual Tables of Maximum Permissible Concentrations (MPC) of the American Conference of Governmental Hygienists are valuable, particularly as the original levels have been altered since 1942, with further experience. Between 1953 and 1957, for example, the MPC of aniline, benzene, butyl cellosolve, iodine, nickel carbonyl and sulphur dioxide have been lowered considerably. Figures for new highly toxic substances have been added, *e.g.* benzyl chloride, chlorine trifluoride, decaborane, diborane, hydrazine, hydrogen peroxide (90%), p-nitroaniline and quinone. Grouping the MPC values suggests that the chemicals likely to cause injury at concentrations of 1, 2 or 3 p.p.m. may be classified as highly toxic, those at 100 to 500 p.p.m. as moderately toxic and those above this as relatively non-toxic. Compounds can be placed in one of these 3 broadly defined groups by the Range Finding Test. Acute toxicity is more accurately established by the more elaborate tests needed to determine the LD50 values. Safe atmospheric concentrations are variously presented as MPC, MAC (Maximal Allowable Concentration), M. safe C. and Threshold Limits, the last being particularly applicable to chronic exposure over an 8-hour working day, but all are assessed on the effect of inhalation. When skin absorption or ingestion are risked, and for chronic toxicity tests, several methods of experimental administration are necessary, and the results should include histological examinations of tissues from those animals which die or are killed.

Biological methods, *i.e.* analyses of blood or urine of compounds or their metabolites, in animals or human beings, have practical disadvantages; they may indicate absorption rather than poisoning, though rising levels may draw attention to increasing exposure. The method of assessing toxicity by clinical examinations and blood examinations, particularly if there has been a pre-exposure standard, though unsatisfactory if used as a trial and error method as sometimes in the past, at times has real value, especially if combined with other methods, and still more so if the results are negative. *M. Patricia Fitzsimons*

SAITA, G. & MOREO, L. Talassemia ed emopatie professionali. Nota I. Talassemia e benzolismo cronico. [**Thalassaemia and Occupational Blood Diseases. I. Thalassaemia and Chronic Benzol Poisoning**] *Med. d. Lavoro.* 1959, Jan., v. 50, No. 1, 25–36, 3 figs. [14 refs.] Nota II. Talassemia e saturnismo cronico. [**Thalassaemia and Chronic Lead Poisoning**] *Ibid.*, 37–44, 3 figs.

The English summaries appended to the paper are as follows:—

I. "Three cases of chronic benzol poisoning are reported, which were characterized by a particular atypical anemic picture and course. Diagnostic difficulties in such cases were overcome only when it was found, through laboratory tests on the patients and their relatives, that the occupational blood disease had developed on a preexisting constitutional blood disorder (thalassemic trait).

"In two of these cases the differences from the usual picture of benzolic blood changes were: marked hypochromia, true microcytosis, marked anisopoikilocytosis, presence of target cells and stippled cells, platelet increase, changes in the hemoglobin (increased foetal and slow adult Hb). The course was similar to that of thalassemic anemias, with chronic anemia for years and transient remission only after large blood transfusions. In the third case, the usual picture of benzolism was modified not only by changes in the morphology of red blood cells, but also by the appearance of hyperhemolysis with splenomegaly, bone marrow erythroblastosis and peripheral reticulocytosis. Furthermore the responsibility of benzol in determining the blood changes was demonstrated by the time relationship between the beginning of hazardous work and the onset of the hemopathy and by the persisting leuco- and neutropenia. In all these cases there were therefore complex blood disorders showing some characters of thalassemia and some of benzol poisoning.

"It is emphasized that the medical pre-employment examination for workers going to be exposed to blood poisons should be compulsorily integrated by an accurate blood examination to be carried out by a competent hematologist, in order to identify subjects with blood disorders compatible with an apparently good health, but that could favour the onset of severe hemopathies after occupational exposure to blood poisoning substances."

II. "Three cases of lead poisoning in subjects with thalassemic traits from the provinces of Ferrara and Rovigo are reported. These workers showed typical signs of lead poisoning, few weeks after the beginning of a hazardous work (colics, anemia). The anemic picture was markedly hypochromic (as is unusual in lead poisoning) with microcytosis, severe poikilocytosis, target cells, increased osmotic globular resistance and it induced to suspect the presence of thalassemia, which was confirmed by familiar tests and by alkali-resistent Hb determination. The high level of coproporphyrins in the urine and protoporphyrin in the blood demonstrated the saturnine component of the anemic picture. Other data, such as the presence of punctated erythocytes, increased blood iron and indirect hyperbilirubinemia are common to both syndromes and therefore cannot be used for a differential diagnosis.

"Removal from the occupational exposure and the usual detoxifying treatments induced a relatively quick regression of anemia (while the constitutional data of definite hypochromia persisted). The course of anemia was not much different from that usually seen in lead poisoning, either for its intensity at the time of heaviest poisoning or for its further course.

"The fact is stressed that these subjects showed early and severe signs of lead poisoning while previously they were in good health even if they were affected by thalassemia traits. It is therefore emphasized that subjects with constitutional blood disorders should not be employed with exposure to lead."

ROFE, P. **The Response to Heinz Bodies in the Rat.** *Brit. J. Indust. Med.* 1959, Jan., v. 16, No. 1, 15–22, 6 figs. [14 refs.]

To assess the significance of Heinz bodies, azogeranine (disodium salt of 8-acetamido-2-benzeneazo-1-naphthol-3 : 6 disulphonic acid) was fed to intact and splenectomized rats at a concentration of 1·5% w/w, and various examinations were carried out during the 2 and 3 months' experiments and for 2 to 5 months afterwards. Beforehand, normal numbers of red blood cells and reticulocytes were found, but no red blood cells containing Heinz bodies. Normal and splenectomized control rats received the same diet without the dye.

In the experimental intact rats the Heinz body red cells rose rapidly within a week to 75%, fell during the 3rd week to fluctuating levels for the next 7 weeks when the dye was stopped, and then disappeared 9 days later; there was a steady fall in the red cells for 3 weeks, followed by a considerable rise during the next 2 weeks and complete recovery about 3 weeks after the dye was stopped, with an even further increase later. In the splenectomized rats there was a similar but more pronounced effect: a higher peak of the Heinz body red cells occurred more rapidly, the fall was slower and smaller, and they took 25 days to disappear when the dye was stopped; the anaemia was more severe, there was no improvement during the experiment and afterwards, though the rate of recovery was almost as rapid as in the intact animals, the red cells final level only reached the pre-experiment level. In both groups there was also a concurrent reticulocytosis.

The livers of the splenectomized rats after chronic induction of Heinz bodies contained large deposits of haemosiderin. There was little or none in the intact rats treated in the same way, nor in splenectomized rats who were not given the dye. Splenic hyperplasia accompanied the initial increase in Heinz body red cells, it remained undiminished after their level had fallen and lasted until the Heinz bodies disappeared. The greatly enlarged spleens showed no microscopic evidence of an increase in the concentration of haemosiderin.

It is suggested that the anaemia and splenomegaly were the response to the presence of Heinz bodies and

not to the direct action of the dye because the anaemia varied according to the level of the Heinz body red cells and was not constant as was the dye intake, and moreover the dye was rapidly excreted, and also because the splenic enlargement did not begin until Heinz bodies were present in substantial numbers and lasted until they disappeared. When one-third of the blood volume was replaced by blood of which 90% of the red cells contained Heinz bodies, normal control rats showed no Heinz bodies after 5 days, but splenectomized control rats took 15 days.

Female rats were fed the dye for 85 days. The anaemia was hypochromic. According to a graph (Fig. 6), the mean cell haemoglobin concentration fell from about 35·7% to 26·7% at the time of peak Heinz body red cell level. With the subsequent fall in Heinz body red cells, approximately one-half this mean corpuscular haemoglobulin concentration deficiency was replaced after 40 days, despite a substantial recovery in the packed cell volume without increase in the red cell count. 20 days after feeding had stopped no Heinz bodies were found and all values had returned to normal. *M. Patricia Fitzsimons*

Tolot, F., Droin & Genevois. Intoxication par la diméthylformamide. [**Dimethylformamide Intoxication**] *Arch. Malad. Professionnelles.* Paris. 1958, Nov.–Dec., v. 19, No. 6, 602–6.

When dimethylformamide was introduced as a solvent in 2 small works where a new synthetic textile was being manufactured, 11 cases of gastric irritation were noticed within 15 months. The workers affected, mainly the spinners and winders, worked an 8-hour continuous shift system with a change over every 2 days, but they had done this kind of shift work before. Vague digestive symptoms—anorexia, nausea, vomiting and a burning sensation in the epigastrium followed by pain and tenderness—were relieved by stopping work but recurred on return to work. Blood examinations and liver function tests were normal, as were X-ray examinations of the stomach (9 cases) and blood urea estimations when carried out. The urine contained no albumin or sugar; in one case bile pigments were present. No respiratory symptoms occurred. Oedema and desquamation, accompanied by itching, were seen in 3 cases, and one had conjunctivitis also; coincidence possibly accounted for enteritis in a spinner whose right hand was so affected. Coincidence also possibly accounted for 3 abdominal attacks, one accompanied by icterus, in a subject who had had jaundice when a child. The predominant gastric and hepatic symptoms were in accordance with the results of animal toxicity tests with dimethylformamide quoted in the article.

The processes, which are described, could not be enclosed, necessitating good general and local exhaust ventilation. Before repair work the plant should be flushed with water. Persons subject to gastric or hepatic disorder, *e.g.* gastritis, ulcer or alcoholism, should be debarred from the workrooms; a 5% solution of acetic or formic acid which seemed to have a curative action on the skin lesions should be available in the workrooms. *M. Patricia Fitzsimons*

Martimor, E., Cavigneaux, A. & Nicolas-Charles, P. J. A propos des troubles mentaux de l'intoxication professionnelle par la nitroglycérine. [**Mental Effects of Occupational Poisoning with Nitroglycerin**] *Arch. Malad. Professionnelles.* Paris. 1958, Nov.–Dec., v. 19, No. 6, 574–80. [19 refs.]

This is largely a review of the literature.

Wolfe, H. R., Walker, K. C., Elliott, J. W. & Durham, W. F. **Evaluation of the Health Hazards involved in House-Spraying with DDT.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 1, 1–14, 4 figs. [13 refs.]

The exposure to DDT of a man spraying a room has been determined under a number of different experimental conditions designed to simulate conditions met with during the application of DDT for mosquito control. Details of practical and effective protective clothing are provided. A 13-litre hand-operated compressor sprayer normally operating with a nozzle pressure of 40 lb. sq. in. was used to apply a 5% DDT formulation to give a deposit of 2 gm. per sq. metre. A 21-in. wand held 15–18 inches from the wall or ceiling was used to apply the spray. Skin contamination and respiratory intake of DDT was calculated from an analysis of the amounts falling on absorbent pads placed on different parts of the body or over the intake of a respirator. Over 1,500 samples were analysed. A man working in an open-necked, short-sleeved shirt without hat or gloves received 1,755 mgm. DDT on the skin each hour while only 7·1 mgm. are inhaled in the same period. It was calculated that under these conditions during a working day in which 4 hours were spent spraying, a dose of 105 mgm./kgm. DDT would settle on such a worker. Exposure is greatest on the front of the neck and chest and on the spraying arm and hand. The amount falling on the skin increases (a) if the nozzle pressure rises, (b) smooth rather than rough walls are sprayed, (c) when ceilings rather than walls are sprayed and (d) environmental temperature rises.

Wettable powders gave slightly more contamination than diluted emulsion concentrates, but the solvents in the latter produced an unpleasant working environment. Cotton clothing provided effective body and limb protection. For the face and neck a veil of green plastic "20 × 20" mesh [presumably 400 holes per square inch] fastened to a helmet was lighter than a transparent vizor. The veil was not rendered opaque by spraying deposit. Details of a pattern are provided. No DDA (a metabolite of DDT) was detected in the urine of a man constantly spraying in this way indicating that less than 3·5 mgm./kgm. per day was being absorbed through the protective clothing.

[The data provided fill an important gap in our knowledge. The need for adequate protection if materials more toxic than DDT are applied in the manner described is made obvious.] *J. M. Barnes*

MATSUYAMA, H. [**Experimental Studies on BHC Poisoning.**] *Shikoku Acta Med.* 1958, June, v. 12, No. 6, 969–97, 6 figs. on pl. [49 refs.] [In Japanese.] English summary.

The evidence suggests a direct harmful effect on the central nervous system, pituitary and suprarenal glands, the parenchyma of various organs and blood cells.

FLETCHER, T. E., PRESS, J. M. & WILSON, D. Bagster. **Exposure of Spray-Men to Dieldrin in Residual Spraying.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 1, 15–25, 1 fig.

A time and motion study of an experienced team of sprayers engaged in a malaria control programme is described. The exposure of the men who were applying 0·55% dieldrin suspensions with stirrup pumps (nozzle pressure 50 lb./sq.in.) was measured by estimating the dieldrin falling on absorbent pads fixed to different parts of the body. An average of 0·65 mgm. dieldrin fell on each 100 cm.^{2} of body surface during a day's work in which 2·1 kgm. dieldrin was applied. The retention of dieldrin by cotton clothing was demonstarted. This is only partly removed by washing in soap and water though washed clothing containing dieldrin did not contaminate pads placed under it on the wearer. Washing in petrol, which is usually available, will remove most of the dieldrin and an occasional wash in petrol in addition to regular laundry is recommended. In contrasting the freedom of this group from poisoning by dieldrin with the occurrence of casualties in other teams the authors point out that poor hygiene, the absence of simple protective clothing and application of higher concentrations of dieldrin may be important factors in causing dieldrin poisoning in sprayers. [A valuable account of how a spray team should apply materials like dieldrin.] *J. M. Barnes*

J. AMER. MED. ASS. 1959, Mar. 21, v. 169, No. 12, 1340–44. [16 refs.] **Prevention and Control of Occupational Dermatitis.** [Report prepared by the Committee on Occupational Dermatoses [BIRMINGHAM, D. J., Chairman] of the Council on Industrial Health, American Medical Association (HOLLAND, B. D., Secretary).]

This is the last in a series of 5 reports prepared by the Committee on Occupational Dermatoses of the Council on Industrial Health of the American Medical Association. It summarizes the views expressed in the 4 earlier reports, and follows the same conventional and unrealistic approach. Industrial dermatitis, they say, is an expensive nuisance; and it could easily be prevented by better enclosure of processes, insistence on cleanliness, washing facilities and changes of contaminated clothing, barrier creams and incentives to use them (otherwise than for the aggravation of an already developed dermatosis), by warning the workman of the chemical hazards of his job, and by excluding from it individuals suffering from acne, lichen planus, psoriasis, seborrhoea and atopic eczema (flexural prurigo).

[Dermatologists in Britain might of course agree that acne vulgaris predisposes to chloracne. But surely the most powerful local remedies are applied to psoriasis with complete impunity and the very characteristic personality associated with atopic eczema is incompatible with self-pity or compensation hunting. A prudent employer might, however, exclude persons with discoid eczema or a history of repeated attacks of acute exudative seborrhoea, not so much because they might be thought to be easily sensitizable to external irritants but for fear that they might at some time be tempted to lay the responsibility for their infirmity on the job.

Of course it is obvious that much chemical damage and allergic sensitization of the skin could be avoided by the successful practice of the above precautions, (though indeed we must all of us have seen cases that could only be described as vicarious or telepathic dermatitis). But in Britain at any rate this constitutes a very small part of the problem. Every industrial medical officer knows that casualties of this kind seldom result in prolonged illness. The real problem is that of people with chronic constitutional dermatoses, convinced often in defiance of all logic that their work is the cause, invaliding themselves and spreading alarm and despondency among their workmates. The workmen should certainly be instructed: in fact a preliminary fortnight spent on a thorough explanation of the work they are going to do, before starting it, is easily the best way of preventing dermatitis; and equally a half-knowledge combines very well with superstition to provoke it.] *J. H. Twiston Davies*

LEVIN, H. M., BRUNNER, M. J. & RATTNER, H. **Lithographer's Dermatitis.** *J. Amer. Med. Ass.* 1959, Feb. 7, v. 169, No. 6, 566–9.

For all practical purposes a lithographer is a workman engaged in printing with etched zinc plates which are often mounted on rollers. The photographic part of the process depends on chromated albumin being rendered insoluble by exposure to light. Printing involves the use of lacquers, solvents such as benzene, turpentine and turpentine substitutes, and much washing of the hands.

53% of a series of 76 cases of dermatitis were pressmen and 23% plate makers. More trouble is experienced on the printing side, no doubt because contact with solvents and excessive washing of the skin renders it more easily sensitizable to the hexavalent chrome which is involved in every stage of the process.

In animal experiments only those guineapigs were sensitized to chrome whose skins had been prepared by some defatting process. Positive patch tests with solutions containing chrome salts at 0·5%–1% were 2 to 8 times as frequent in workmen with active eruptions or a history of dermatitis as in those not complaining of their skins. Possibly 0·5% is too high a concentration for this purpose, especially in view of reports that many patients with spontaneous eczematoid dermatoses react to it. It may also be that the conventional closed type of patch test is an unsatisfactory means of investigation.

One of the difficulties in prevention is that we are dealing with a skilled craft in which the mediation of protective gloves and instruments must impair the expertise of manipulation, and the nature of the process clearly excludes the use of barrier creams. Nevertheless one could imagine ways of cleaning the plates and other parts of the press other than by means of a handful of solvent-soaked rag.

Although the question why workmen sufficiently exposed to chrome to develop ulcers and septal perforations do not often become allergic is not canvassed, the conclusion reached is that the subject cannot possibly be as simple as it might appear to be at first sight. *J. H. Twiston Davies*

OSHIMA, T. [**The Dermatitis developed specifically on the Feet of Coal Mine Workers.**] *Igaku Kenkyu.* Fukuoka. 1958, Dec., v. 28, No. 12, 4796–802, 6 figs. [31 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"The author found that the dermatitis peculiar to the feet in colliery workers has its causal agents in the coal dust, the gushing water and the particles of rock and stone which abound in the pits the workers are employed in and which mechanically injure the skin, and in the sulfuric acid which is formed by the coal dust and the water and which is causative of the ulceration characteristic of this type of dermatitis."

ARCH. MALAD. PROFESSIONNELLES. Paris. 1959, Jan.–Feb., v. 20, No. 1, 34–78. [Numerous refs.] Journée d'études des matières plastiques, Paris, 22 mars 1958. [**Conference on Plastics**]

Manufactured plastics are never volatile; they are either infusible or have no particular melting point; many of them are insoluble. They are formed by condensation of simple monomers or of pairs of complementary monomers combining with release of water; some are composed of mixtures of different monomers.

They fall into the 2 main classes, *viz.* thermoplastic [*e.g.* Perspex, a liquid solidified by exposure to radiant energy], and thermostable [*e.g.* Bakelite, a powder moulded under the influence of heat and pressure].

Monomers, with the possible exception of Styrolene, and finished products, are usually harmless to the skin; but some of the raw materials, *e.g.* phosgene formaldehyde and phenol, are obviously dangerous, and many of the plasticizers, accelerators and antioxydants have been responsible for sensitization phenomena.

M. VIEUX (pp. 39–43) states that 86 of the 100 days lost by workers in a process employing about 500 was attributable to mechanical damage to fingers and hands. L. TRUFFERT (pp. 43–50) mentions an obscure toxic reaction by workers in polyvinyl plastics; but he is mainly concerned with the toxicological possibilities of certain additives such as accelerators and colouring matter, and of certain products of combustion. In particular he calls attention to the rumour that it might be fatal to smoke a cigarette contaminated with polytetrafluoroethylene. But animal experiment failed to confirm the possibility. (Most fatal accidents by inhalation of the products of combustion of plastics have been due to the nitric oxides liberated by the combustion of photographic film.) As for the danger of cooking vessels enamelled with this plastic, C. TROYANOWSKY (pp. 57–60) states that decomposition is slight below 300°C., a temperature too high to be used in cooking. Only the phosphorus, chrome or other materials added to the plastic to secure its adhesion to the metal could possibly be harmful.

Industrial medical officers complain of their difficulties in obtaining particulars of the composition of plastics and related products supplied under trade names. But, by and large, little skin trouble has with any certainty been attributed to products other than the formaldehyde-phenol glues, uncured powders in the same group, and of course the whole family of epoxy resins. M. S. TARA (pp. 67–70) believes that, with simple precautions of cleanliness, all trouble with epoxy resins could easily be avoided. On the other hand M. A. SIBOULET (pp. 71–73) attributes most of the trouble to vapour evolved by mixtures of araldite and hardener used hot. This not only attacks the skin but also causes fever and gastro-intestinal disturbances. He recommends protection of the skin by means of an aerosol suspension of silicones. M. GAULTIER, E. FOURNIER and C. GUYOTJEANNIN (pp. 75–78), reporting 16 cases from a hospital department of industrial medicine, complain of their isolation from the industrial medical officer and his work. Of the 16 cases reported by these workers 6 had irritation of the skin, 4 of the respiratory tract, 4 of the gastro-intestinal tract, nearly all in connexion with phenol-formaldehyde plastics; and one presented with signs of damage to the bone marrow, thought to have arisen from the careless use of benzol in preparing moulds.

J. H. Twiston Davies

INTERNAT. COMMISSION ON RADIOLOGICAL PROTECTION. **Recommendations of the International Commission on Radiological Protection** (adopted September 9, 1958). [SIEVERT, R. M., Chairman]. pp. vi + 18. 1959. New York. Paris. Los Angeles. London: Pergamon Press Ltd., 4 & 5 Fitzroy Square, W.1. [3s. 6d.]

This Commission functions under the auspices of the International Congress of Radiology; at the same time it is formally affiliated with WHO as a non-governmental participating organization.

This brief report is so packed with matters relevant to radiation protection that to abstract it would be inappropriate and in lieu of this a summary of the various sections is listed for the reader as follows:—

A. Prefatory Review. This goes over the ground previously covered, but with reasons for modifying the various permissible dosage data.

B. Basic Concepts. Here are discussed the various critical organs and tissues and the categories of exposure to which they may be subjected.

C. Maximum Permissible Doses. These depend on the tissues in question, whether the irradiation is from within the body or external to it. A subsection is devoted to the questions relating to

exposure to radiation of the whole population of a country.

D. General Principles regarding working conditions. The first principle laid down is that the owner or person in charge of a controlled area shall be responsible for the working conditions. During and after installation appropriate radiation surveys shall be made to ensure that the pertinent recommendations will be complied with when routine operations begin. *S. Russ*

BOONE, Irene U., ROGERS, Betty S., WHITE, D. C. & HARRIS, P. S. **Toxicity, Excretion and Tissue Distribution of Ionium (Th^{230}) in Rats.** *Amer. Indust. Hyg. Ass. J.* 1958, Aug., v. 19, No. 4, 285–95, 7 figs. [10 refs.]

This study was undertaken because of the increasing use of ^{230}Th as a tracer for natural thorium and of its associated hazards in uranium ore processing.

Rats were injected intravenously and elaborate observations made upon the urine and faeces in tracing the elimination of the toxic element, some of which, however, was deposited in the body. Approximately one-third of the retained ionium was in the skeleton and two-thirds in the soft tissues; of the latter 20 to 30% was found in the liver.

The authors contrast the behaviour of this radionuclide with that of plutonium, which had already been studied in the same laboratory. Interesting differences were revealed by means of autoradiographics made of various organs selected. Some of these differences are explained by the predilection of ionium for cells of the reticulo-endothelial system. There was, however, a similar pattern of deposition in the liver and spleen. Kidney radio-autographs have shown plutonium to be concentrated primarily in the papillary region, while ionium was confined to the cortex.

The authors conclude that although there are differences in the reaction of the body of the rat to these 2 substances, there are sufficient similarities in their general toxic effects to recommend that permissible levels for ionium exposure be the same as those for plutonium. *S. Russ*

Atmospheric Pollution

KALYZHNIY, D. N. **[The Effect of Air Pollution with Discharges from Metal Works on the Health of Children]** *Gigiena i Sanitariya.* Moscow. 1959, v. 24, No. 2, 3–7. [In Russian.]

The English summary appended to the paper is as follows:—

"The author has investigated the pollution of the atmospheric air in the districts with metal works and its effects on the general sanitary conditions and the health of the population.

"The results of the investigations show that the lungs of the children living in the vicinity of metal works are in a worse state than those of children of the same age from settlements, where the air was free from industrial discharges. The children of the former group suffered from diseases of the upper respiratory tract twice as often as those of the latter group. The author proposes general measures for diminishing the harmful effect of the discharges from metal works and improving the sanitary conditions of living in their vicinity."

The author gives a table of the results of an X-ray examination of 985 children from 2 polluted areas and 2 control areas. In 31·4% and 27% of children in the polluted areas, as compared with 18·3% and 4·3% in the control areas, the lung pictures showed, besides changes in the hilar glands, changes in the pleura (interlobar and pleural adhesions) and in the lung tissue itself, while the worst cases showed the first stages of coniosis.

The following is a translation of Table 4:—

"Diseases of the upper respiratory tract in relation to the pollution of the atmosphere"

Disease	Test Area	Control Area
Chronic catarrhal rhinitis	37	10
„ hypertrophic rhinitis	13	3
„ atrophic rhinitis	3	10
Acute rhinitis	3	–
Chronic rhinopharyngitis	7	7
„ catarrhal pharyngitis	6	1
„ granular pharyngitis	10	–
Atrophic pharyngitis	–	11
Hypertrophic pharyngitis	–	2
Catarrhal tonsillitis	33	5
Hypertrophic tonsillitis	–	3
Hypertrophy of the tonsils	–	3
Total of diseases	112	55
Total of children examined	176	185
Incidence of disease at single examination	63%	30%

Hygiene of Buildings

HOUSING AND BUILDING CONSTRUCTION

DEPT. OF HEALTH FOR SCOTLAND. **Designing for Safety in the Home.** 16 pp., illustrated. 1958. Edinburgh: H.M. Stationery Office. [1s. 3d.]

In Scotland in recent years there have been over 1,000 home accident deaths annually. This booklet, prepared for the Department of Health for Scotland by the Central Office of Information, has been compiled particularly for "architects and other technical officers as well as for members of Housing Committees and others interested in home safety." The recommendations are primarily concerned with securing safety in the design and construction of new houses but some of them are applicable to existing houses.

The subject matter is clearly and simply set out with a few drawings to illustrate how some of the commoner accidents occur in different parts of the house. In the recommendations which are made in respect of structure and design there is particular stress on the importance of carrying out electrical wiring in accordance with existing regulations. "Electrical accidents are almost always due either to defective portable appliances or their flexible leads or to temporary wiring put in by the tenants." *M. E. Delafield*

HEAT REGULATION, VENTILATION AND LIGHTING

J. INST. HEATING & VENTILATING ENGINEERS. 1959, Jan., v. 26, 257–71, 2 figs. **Discussion on the Ventilation of Operation Theatres** [COX, W. R., Chairman].

This discussion, which was opened by a communication by Dr. R. BLOWERS and Dr. K. R. WALLACE, should not only clarify what are the problems of ventilating operating theatres but should also dispel any notion that these have all been solved or are about to be. Blowers and Wallace described the dangers of simple exhaust systems of ventilation—still widely used—and the advantages of delivering by a plenum system, under positive pressure, air from outdoors which was warmed and filtered before being admitted near the ceiling. Plenum ventilation systems actually installed in operating theatres show a wide range of efficiency. Often their effective ventilation rate, measured by the speed with which they remove a known number of air-borne bacterial particles, may be surprisingly increased by quite simple modifications. The problems have now been studied both in real operating theatres and in an experimental theatre, of which details are given. Air comes into the experimental theatre through 6 rectangular openings in the ceiling. Ventilation is most effective if the incoming air is some 15°F. warmer than the air already in the theatre and if it is projected horizontally by appropriately designed distributors just below the inlets. The best means of outlet proved to be one outlet point on each of the 4 walls, mid-way along and as close to the floor as possible. 3 outlets on one wall only gave fairly good results; fewer than this were not satisfactory. The best type of the outlet was a 12-in. square hole covered on the outside by a flap of 16-gauge aluminium with a simple fabric hinge along the top edge. These were better than forced extraction by fan because when the theatre door was opened and pressure in the room dropped, the flaps instantly closed so that all the ventilation air passed out of the theatre through the door, preventing the entry of contaminated air from outside.

With 12–15 air changes an hour, and all conditions optimal, the *effective ventilation rate* (defined in the paper) was equivalent to what would be produced by 30–40 air changes an hour.

The discussion showed, among other things, the many complex technological issues still unsolved, the possible need for an operating theatre to be a room within a room, and the importance of appointing and consulting a ventilating engineer at an early stage in the construction of any new operating suite. Too often the heating and ventilating engineer is called upon at a late stage and asked to ventilate a theatre whose siting and construction have already been fixed in such a way as to make the outcome unsatisfactory whatever ingenuity is displayed. *J. W. Howie*

BEDFORD, T. **Heating in relation to Human Comfort.** *Heating.* 1958, Sept., v. 20, No. 154, 286–8.

This is a general account of the subject.

Sanitation

WATER AND SWIMMING BATHS

(Including the bacteriology of water supplies)

ZIMMERMANN, W., RHEINFURTH, H. & SCHWILLE, F. Trinkwasser und Teerprodukte. [**Drinking Water and Tar Products**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 1/2, 155–64, 8 figs. (1 coloured on pl.). [10 refs.]

This paper contains a detailed account of the investigations which were carried out as a result of complaints from a community of about 200 persons in the Eifel district that the water supply not only tasted and smelt of tar but also that consumption of the water had led to intestinal disorders. It was ultimately proved that a well and a water reservoir were heavily contaminated by tar residues from a factory. The findings of the investigations are fully described with a plan of the factory in relation to the water supply, and photographs of the well and the oily deposit on sampling bottles. The geology of the area, the technical processes carried out at the factory and the results of chemical and bacteriological analyses of the water are reported. It was found that considerable amounts of oil could be extracted from the water by treatment with ether and that volatile and non-volatile phenols were also present.

The increasing importance of the possible pollution of water supplies by tar and oil products is stressed and there is some discussion of the mechanism, which is not yet fully understood, whereby these products penetrate through the soil. *M. E. Delafield*

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

CORNELSON, D., SECHTER, I., BĂLTEANU, E. & AVRAM, V. La pollution bactériologique spécifique des cours d'eaux par les résidus des usines de pénicilline. [**Contribution to the Study of the Specific Bacteriologic Pollution of Natural Basins by Sewage from a Penicillin Plant**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, June, v. 17, No. 2, 271–8, 3 figs.

This paper from the Institute of Hygiene at Iassy, Rumania, reports the results of examining the effluent from a penicillin factory, the effluent of the town sewer, and the water of a river into which both are discharged. Comparison of the 2 effluents showed a total bacterial content of a similar order, but of a different nature. The factory effluent consisted chiefly of Gram-negative bacilli, including *Pseudomonas* species and when cultivated quantitatively in media containing 1, 10, 100 and 1,000 units/ml. of penicillin yielded 100, 90, 65 and 33% respectively of the numbers of colonies obtained in normal medium. The town sewage contained relatively much larger numbers of colonies of Gram-positive cocci, and the percentages of the total flora resistant to the aforementioned concentrations of penicillin were only 48, 24, 10 and 3 respectively. A larger proportion of the factory effluent resistant organisms were also resistant to 10,000 units/ml. and produced more penicillinase than those from the sewer: this penicillinase was extracellular, whereas that from the sewer strains was not [the quantitative data on penicillinase production are unconvincing, and the tests for free penicillinase are so briefly described that the surprising conclusion from them must be accepted with reserve].

Perhaps the most interesting findings reported are the numbers of organisms resistant to 1,000 units/ml. of penicillin at various points in the river itself. Above the factory 0·7% of the total flora exhibited this resistance; 3, 9 and 19 km. below it the percentages were 30, 8 and 5 respectively; thus these resistant organisms travelled in diminishing numbers to a great distance. *L. P. Garrod*

MIZUNO, W. G., ROGERS, M. R. & KAPLAN, A. M. **Development of a General Purpose Disinfectant for Military Use.** *Soap.* New York. 1958, Dec., v. 34, No. 12, 105–11, 257–8; 1959, Jan., v. 35, No. 1, 99–106. [18 refs.]

The only purpose discussed in this paper is the disinfection of latrine buckets. In order to safeguard both the user and those emptying the contents of these buckets it is considered necessary to disinfect only their liquid contents: bacteria in solid faeces may safely remain unaffected. Such a disinfectant should be in concentrated powder form to facilitate transport. A method of test was devised on the following basis. Nitrogen estimations were carried out on solid and liquid faeces from which it was calculated that a mixture of the two contains about 5% of protein; tests were therefore carried out in the presence of 5% peptone. [A simple solution cannot be accepted as the equivalent in organic matter of faeces, which is immensly varied in nature and largely particulate, but some of the findings by this method were confirmed with actual faeces.] In tests mainly done with *Escherichia coli* various halogen disinfectants and quaternary ammonium compounds were found unsatisfactory, but phenol derivatives gave better results and the eventual choice fell on a mixture containing 75% sodium chloro-*o*-phenyl phenate and 25% sodium-*o*-phenyl phenate. It is concluded that this should be added in a concentration of 2,000 p.p.m. Data are furnished on the stability of this disinfectant and on its activity in the presence of other materials, particularly soaps.

L. P. Garrod

Food and Nutrition

FOODSTUFFS

Composition and Bacteriological Control

ŠVEC, J., with the technical assistance of KLÍMOVÁ & ŠAŠKOVÁ. Přežívání mikroorganismů na papírových a parafinových obalech. [**Survival of Micro-organisms on Paper and Waxed Paper Wrappers**] *Českoslov. Hyg.* Prague. 1958, v. 3, No. 6, 341–7. English summary.

An investigation has been made of the possibility of bacterial contamination of paraffin wax containers used for packaging foodstuffs. In 986 smears taken from paper stocks, hands of operating staff and machinery *Escherichia coli* was found in 3 instances, *Streptococcus pyogenes* in 4, *Proteus* species in 11 and a β-haemolytic streptococcus in 1 instance. The containers were waxed by dipping them in a bath of paraffin wax at 95°C. for 10 seconds, with subsequent drying at 112°C. for 120 seconds, and the effect of this process on the viability of bacteria was studied. Among a group of 13 common pathogenic and other bacteria exposed to this treatment under laboratory conditions only aerobic sporing bacteria survived the treatment. Organisms placed on sterile waxed containers remained viable for at least 30 days. *D. J. Bauer*

SMITH, J. **Milk-Borne Disease.** *J. Dairy Res.* 1959, Feb., v. 26, No. 1, 88–104. [94 refs.]

This long paper on milk-borne disease is in the series of "Reviews of the Progress of Dairy Science". It contains a long review of the subject based on an impressive number of recent papers, official reports and books. Although the safety of the milk supply has been much enhanced, yet much criticism can still be levelled at the methods in use for its control. Modern experiences of milk-borne infections and their investigation as recorded in the references are here surveyed and summarized. The diseases which are considered in separate sections are: tuberculosis, salmonella infections (a. typhoid and paratyphoid fevers, and b. food poisoning), dysentery, staphylococcal infections, brucellosis, leptospirosis and Q fever. "No new investigations on the possible transmission of virus diseases have been published." *M. E. Delafield*

CAMPBELL, J. E., MURTHY, G. K., GOLDIN, A. S., ROBINSON, H. B., STRAUB, C. P., WEBER, F. J. & LEWIS, K. H. **The Occurrence of Strontium-90, Iodine-131, and Other Radionuclides in Milk—May, 1957 through April, 1958.** *Amer. J. Pub. Health.* 1959, Feb., v. 49, No. 2, 225–35. [26 refs.]

This report summarizes the findings of a U.S. Public Health Service laboratory group engaged in determining specific radionuclide activity in milk samples from 5 areas of the U.S.A. The aims were to develop and simplify methods of radiochemical analysis for milk, to make them more suitable for use by state and local health departments. The chief radionuclides are strontium-90 and cesium-137 of comparatively long life and iodine-131, barium-140 and strontium-89 of shorter durations.

Another interest in this study was to see whether the amounts of these milk contaminants varied with the amounts of radio-active fallout associated with the U.S.A. weapon tests (atomic).

This has been a very elaborate and well designed investigation and a considerable degree of expertness is evident in the radiochemical methods of separation of the various nuclides and their subsequent quantitative estimations. Here are collected in tabular form the results of these analyses of monthly milk samples collected over a 12-month period.

The general conclusion drawn by the authors is that no correlation was found in the amounts of the long-lived radionuclides and the frequency of the weapon tests, but there was for the shorter-lived ones. This difference is doubtless linked up with the actual time for which the fallout is in the atmosphere.

The authors advocate an extension of this kind of analysis in order to evaluate the significance of these radionuclides in our over-all radiation exposure.

S. Russ

FOOD POISONING

BJERKE, O., ERIKSEN, O. R. & LUNDE, S. Botulisme fra Rakörret. [**Botulism from Salted "Rak"—Treated Trout**] *Tidsskr. f. d. Norske Laegeforen.* 1959, March 1, v. 79, No. 5, 249–51.

Trout caught in large quantities in distant waters in Norway are sometimes gutted on the spot, the internal organs slashed and the flesh flattened by slitting and then lightly salted in preparation for packing closely out of contact with the air. To this end a weak solution of salt can be superimposed. In February 1957 a man aged 34 ate plentifully of this delicacy with 4 companions, none of whom fell ill. A day later he felt unwell and vomited violently. His mouth and throat felt very dry, and after 6 days visual disturbances set in. On February 11 an oculist diagnosed accommodation paresis which was still demonstrable 3 days later when the pupils reacted to light less well than they had done and the dryness of mouth and throat had increased. There was also a hint of anisocoria and nystagnoid movements on glancing to either side. The patient's blood contained small quantities of type B botulinum toxin, and a similar toxin was found in the offending fish. The eye symptoms vanished suddenly on March 14, since when there have been no other signs of botulism. It is possible that the fish became contaminated with *Clostridium botulinum* while it lay on the ground before undergoing the *rak* ritual

(as described above) or that the process of gutting had slashed the intestines and thus brought their contents into contact with the flesh of the fish. Hitherto Norwegian publications about botulism have concerned human beings who suffered from it after eating pickled pork or home-canned meat cakes. So far *rakörret* [trout treated as described] seems to have escaped notice in this respect, in Norway at any rate.

Claude Lillingston

CLARENBURG, A., KAMPELMACHER, E. H., VAN KEULEN, A. & DE NOOY, E. Epidemiologische bevindingen bij een vleesvergiftiging, veroorzaakt door *Salmonella typhimurium*. [**Epidemiological Findings on an Outbreak of Food Poisoning caused by the Contamination of Meat with** *Salmonella typhimurium*] *Nederl. Tijdschr. v. Geneesk.* 1958, Oct. 25, v. 102, No. 43, 2095–7. English summary (5 lines).

In February 1957, 17 persons developed food poisoning after eating preserved meat from a home-killed pig which was apparently healthy. The illness was characterized by high fever, vomiting and diarrhoea, and 7 persons required treatment in hospital. *Salmonella typhi-murium* was isolated in large numbers from samples of the remaining meat, from the stools of 4 patients and also from mice and a cat with which the pig had been in contact during life. All strains isolated were of fermentation type 10. *D. J. Bauer*

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

MORSE, M. L. & ALIRE, M. L. **An Agar Medium indicating Acid Production.** *J. Bacteriology.* 1958, Sept., v. 76, No. 3, 270–71, 1 fig.

For the detection of fermentative variants in genetic studies the following medium was evolved: Sigma *p*H 7–9 tris(hydroxymethyl)aminomethane buffer, 1.3 gm., dehydrocholic acid, 1·5 gm., Difco yeast extract, 1·0 gm., Difco proteose peptone, 10·0 gm., agar, 12 gm. and neutral red, 0·075 gm. per litre. The reagents are dissolved in this order and 1% of the chosen carbohydrate included. The final *p*H should be 7·6.

It should be noted that the substitution of phosphate buffers for the Sigma 7–9 buffer destroyed the usefulness of the medium.

The final medium is pale red, colonies of fermenters are dark red and non-fermenters white.

The medium was valuable in studies of *Escherichia coli* and *Staphylococcus aureus* variation. It could be used for *Streptococcus faecalis* and, with less neutral red and dehydrocholic acid, appeared satisfactory for a pneumococcus. *J. Nagington*

KOSUNEN, T. & PARMALA, M. E. **Use of Phenolphthalein Phosphate-Chromate Plate as a Selective Isolation Medium for Micrococci.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1958, v. 36, No. 4, 356–9.

Phenolphthalein-phosphate-chromate plates [this *Bulletin*, 1957, v. 32. 198] were used as a primary isolation medium for specimens containing staphylococci and *Proteus vulgaris*, *Pr. mirabilis* and *Pseudomonas pyocyanea*. Staphylococci were isolated more times (× 3, × 6 and × 2 respectively) from samples containing the corresponding Gram-negative rod in 1956–7 when this medium was included than in 1953–4 when conventional media only were used. The authors believe that this increase is due mostly to the use of this selective medium. *M. Patricia Jevons*

GHOSH, S., ROY, Dolly & GUHA, B. C. **Effects of Some Folic Acid Analogues on the Growth of** *S. faecalis*, *L. arabinosus* **and** *E. Coli*. *Ann. Biochem. & Exper Med.* Calcutta. 1958, v. 18, No. 5, 161–74, 8 figs. [27 refs.]

PIRT, S. J. & CALLOW, D. S. **Observations on Foaming and its Inhibition in a Bacterial Culture.** *J. Applied Bact.* 1958, Dec., v. 21, No. 2, 211–16, 1 fig.

MCCARTY, M. **The Occurrence of Polyglycerophosphate as an Antigenic Component of Various Gram-Positive Bacterial Species.** *J. Exper. Med.* 1959, Apr. 1, v. 109, No. 4, 361–78, 4 figs. [10 refs.]

International Code of Nomenclature of Bacteria and Viruses. Bacteriological Code.

This book was reviewed on p. 592.

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order: General; Antibiotics; Other Therapeutic Substances; Disinfection.

WOLSTENHOLME, G. E. W. & O'CONNOR, Cecilia. M. **Ciba Foundation Symposium on Drug Resistance in Micro-Organisms. Mechanisms of Development.** pp. xii + 352, 62 illustrations. [Numerous refs.] 1957. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [50s.]

The symposium of which this volume is a report took place in London on March 26–28, 1957. Among 31 participants there were representatives of 7 European countries as well as of Great Britain and the United States. It includes 18 papers and full—apparently verbatim—reports of discussions on them and of a general discussion with which the meeting concluded. The subject was chosen not only because acquired microbic resistance seriously threatens the practical utility of many drugs, and may conceivably be a change capable of being brought under some kind of control, but because its study may contribute to converting chemotherapy from a largely empirical to a more rational subject.

The nature of the change producing increased drug resistance being the central question under discussion, many contributions necessarily dealt with the long-standing controversy on whether this change results from adaptation or mutation. The opening paper by A. C. R. DEAN and C. HINSHELWOOD (pp. 4–29) argues in favour of the former: the majority of subsequent speakers including M. DEMEREC, L. L. CAVALLI-SFORZA and H. EAGLE supported the mutational hypothesis, the last declaring himself a recent convert to it, while others contend that more than one mechanism may operate. Several contributions deal with changes in bacterial metabolism associated with drug resistance, and with the general subject of bacterial genetics as it affects this problem. There are few references to clinical aspects of the subject, and no conclusions of practical application were reached except some expressed in general and tentative terms by J. LEDERBERG in the concluding discussion. This volume is a valuable source of detailed information on fundamental studies of bacterial behaviour which should ultimately contribute to clarifying the subject of the symposium.

L. P. Garrod

SUTER, L. S. & ULRICH, Elizabeth W. **Routine Bacterial Sensitivity Studies.** *Antibiotics & Chemotherapy.* New York. 1959, Jan., v. 9, No. 1, 38–46.

This paper analyses the results of 7,858 tests of sensitivity to antibiotics of 984 strains of bacteria isolated in a 2-year period at the Veterans Administration Hospital, Memphis, Tenn. These are divided into 9 varieties of common bacteria, 4 being Gram-positive cocci (micrococci, enterococci, pneumococci and *Streptococcus viridans*) and 5 coliform bacilli: 32 strains referred to as "others" included all *Str. pyogenes, Haemophilus* and *Bacteroides* as well as 6 other named varieties of organism: that there should have been so few of some of these is surprising. Of the 13 agents tested, which included the principal antibiotics, 2 antibiotic mixtures and 2 synthetic compounds, some were employed in a tube dilution test, the arbitrary limit of sensitivity being inhibition by 12·5 μgm./ml., others by a disk method, the content of the disk being 10 μgm. for some antibiotics, and less or more for others [it is not clear how the method was chosen for each drug, and no technical details are given]. The table giving the complete results is rather difficult to follow, because it is continued overleaf without repetition of side headings, but in general the findings are what might be expected from tests adopting these criteria, which seem to favour drugs tested by the dilution method and set a decidedly low standard of sensitivity. The most original observations are those which relate sensitivity to bodily source. Staphylococci were more often sensitive to penicillin and tetracycline when isolated from bone than from wounds or the air passages. This is thought to be due to "the greater frequency of chronic pulmonary conditions that have been treated with penicillin" [but another explanation might be that osteomyelitis usually arises outside the hospital, where resistant strains are less common]. Enterococci and *Pseudomonas* isolated from the ear were much more often sensitive to tetracyclines than when isolated from the urinary tract or wounds: this is attributed to "a lack of chronicity in most ear infections", but here it may be doubted whether the infections were the same. It is admitted that enterococci were rarely identified to species level and nothing is said about classifying *Pseudomonas* species.

L. P. Garrod

BRAUSS, F. W. Experimentelle Untersuchungen zum Problem der Resistenz-Erhöhung [**Experimental Investigations on Bacterial Resistance**] *Arch. f. Hyg. u. Bakt.* 1959, Feb., v. 143, No. 2, 140–44.

In the author's view, the possibility of destroying staphylococci by chemical means outside the body have been somewhat neglected in attempts to prevent hospital infection. But first it is necessary to be sure that staphylococci resistant to antibiotics are not also abnormally resistant to disinfectants. He therefore tested strains of *Staphylococcus aureus* and *Escherichia coli* resistant to one or more antibiotics with a chlorophenol disinfectant and an ampholyte soap and found them as susceptible to the bactericidal action of these substances as antibiotic-sensitive strains. He also showed that bacterial resistance does not develop to Tego 103S (an ampholyte soap) (1) by 50 transfers of *E. coli* in medium containing this disinfectant, (2) by comparing the flora of industrial and other environments where this disinfectant is used with that of similar places where it is not: resistant strains were not found in the former.

L. P. Garrod

OSKAM, H. J. & KOELMAN, A. **Application of Logarithms to the Base 2 in the Use of Exponential Dilution Series for the Study of Antibiotic Combinations.** [Correspondence.] *Nature.* 1959, Mar. 21, v. 183, 840–41, 1 fig.

See also p. 651, CORNELSON, SECHTER, BĂLTEANU & AVRAM, La pollution bactériologique spécifique des cours d'eaux par les résidus des usines de pénicilline. [**Contribution to the Study of the Specific Bacteriologic Pollution of Natural Basins by Sewage from a Penicillin Plant**]

HYMAN, A. L. **Anaphylactic Shock after Therapy with Penicillinase.** *J. Amer. Med. Ass.* 1959, Feb. 7, v. 169, No. 6, 593–4.

Penicillinase functions by hydrolysing penicillin to the antigenically inert penicilloic acid. It has been given to human beings to counteract the effects of a penicillin reaction, usually without any serious untoward effects. The author describes a case in which the administration of penicillinase by intramuscular injection resulted within 2 minutes in a very severe reaction in the patient, a 50-year-old woman suffering from a penicillin reaction. The patient complained of weakness, dizziness and dimness of vision and this was followed by orthopnoea and cyanosis. Pulse and blood pressure were unobtainable and heart sounds were irregular at 30 to 40 beats per minute. The patient was treated with epinephrine, prednisone, meperidine and oxygen and made a good recovery. *A. B. Christie*

REISCH, M. **Penicillinase Therapy—Clinical Report of Severe Reactions.** *J. Amer. Med. Ass.* 1959, Feb. 7, v. 169, No. 6, 594–5.

A patient suffering from a penicillin reaction was given penicillinase intramuscularly and intravenously. An hour later he had a rigor, dyspnoea and cyanosis. He was treated with adrenocorticotrophin with some success but continued to have weals and was given a second dose of penicillinase. On this occasion he had no febrile reaction but considerable local swelling and pain.

A second patient with a penicillin reaction was treated with penicillinase intramuscularly. He developed local pain and swelling, a rise in temperature and was semicomatose for 12 hours. Urticaria persisted and he was given a second injection of penicillinase: he developed nausea, chills and fever and slept for 30 hours. The author considers that in extremely young children, in the debilitated and in the aged who may not tolerate respiratory or cardiac embarrassment, penicillinase should not be used. *A. B. Christie*

ALLEGRA, G., NIUTTA, R. & GIUFFRIDA, G. Influenza del cloroamfenicolo sullo sviluppo e sulla composizione degli aminoacidi liberi e combinati della Salmonella Bareilly. [**Influence of Chloramphenicol on the Development and Composition of the Free and Combined Amino Acids of Salmonella Bareilly**] *Riv. Istituto Sieroterap. Ital.* 1959, Jan.–Feb., v. 34, No. 1, 47–55, 1 graph. [31 refs.] English summary (6 lines).

SWEENEY, W. M., HARDY, S. M., DORNBUSH, A. C. & RUEGSEGGER, J. M. **Demethylchlortetracycline: A Clinical Comparison of a New Antibiotic Compound with Chlortetracycline and Tetracycline.** *Antibiotics & Chemotherapy.* New York. 1959, Jan., v. 9, No. 1, 13–22, 6 figs.

Demethylchlortetracycline differs from chlortetracycline in the absence of a methyl group in the 6 position. It is much more stable to acid and alkali than other tetracyclines, but otherwise has similar properties including low toxicity and high therapeutic activity. The only particulars given here of its antibacterial activity refer to action on *Staphylococcus aureus*: against this organism it has 75% of the activity of chlortetracycline, whereas tetracycline is credited with only 25% of this and oxytetracycline 24%.

The paper otherwise reports only pharmacological studies. Single doses of 3 tetracyclines were given to normal adults and the antibiotic was assayed in the blood after 1, 3 and 6 hours, and in the urine. The findings are somewhat complicated by expression in 2 ways: in terms of μgm./ml. of the respective substance, the highest levels then being given by tetracycline, and in terms of antimicrobial activity (tetracycline equivalent), the highest levels then being given by chlortetracycline. In both the levels of demethylchlortetracycline are intermediate. In a further experiment demethylchlortetracycline only was given in a dose of 250 or 500 mgm. and blood was assayed at intervals up to 24 hours and thereafter at 2, 3, 4 and 5 days. In this it was shown that this drug persists remarkably in the blood: all samples examined after 3 days contained it (average content as tetracycline equivalent 0·15 or 0·28 μgm./ml. according to the dose given) and most contained some after 4 or 5 days. The slow excretion observed by KUNIN and FINLAND [this *Bulletin*, 1959, v. 34, 369] is believed to account for this.

L. P. Garrod

KUNIN, C. M., WILCOX, Clare, NAJARIAN, Ann & FINLAND, M. **Susceptibility and Cross-Resistance of Bacteria to Four Related Antibiotics: Kanamycin, Paromomycin, Neomycin and Streptomycin.** *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 312–16, 3 figs.

The work described here shows a very close relationship in antibacterial behaviour between kanamycin, neomycin and paromomycin (Humatin, formerly Humycin). The minimum inhibitory concentration of each of these antibiotics was determined for large numbers of strains of staphylococci and of 6 varieties of coliform bacilli, with closely concordant results. When 2 strains of staphylococci and 1 of *Klebsiella pneumoniae* and 1 of

Escherichia coli were rendered resistant to each antibiotic by the usual *in vitro* procedures, they became in each case about equally resistant to the other two. Cross-resistance between these antibiotics was also observed in resistant strains of faecal coliform bacilli recovered from patients treated orally with kanamycin or paromomycin.

Streptomycin was included in all these tests, and a much less close relationship between it and the other 3 is demonstrated. Many of the numerous stock cultures tested were resistant to streptomycin, although sensitive to the other 3: streptomycin was also less generally active against staphylococci and more so against *Pseudomonas* spp. Cross-resistance artificially produced was only partial, and some of the faecal organisms resistant to the other group after treatment with one of them remained sensitive to streptomycin.

L. P. Garrod

i. Margalith, P., Beretta, G. & Timbal, M. T. **Matamycin, a New Antibiotic. I. Biological Studies** *Antibiotics & Chemotherapy*. New York. 1959, Feb., v. 9, No. 2, 71–5, 1 fig.

ii. Sensi, P., Ballotta, R. & Gallo, G. G. **II. Isolation and Characterization.** *Ibid.*, 76–80, 2 figs.

These 2 papers from the Research Laboratories of Lepetit, Milan, record the isolation of an antibiotic from *Streptomyces matensis* n.sp.: this organism was recovered from "a soil sample of sea sand" collected in Catania, Sicily. A description is given of this organism, of the methods used in cultivation and extraction, and of the physical and chemical properties of the antibiotic, matamycin. This is a substance of very low solubility, contains sulphur, and is very unstable in acid solution. Its minimum inhibitory concentrations for 8 species of bacteria are stated: it is more active against Gram-positive than Gram-negative organisms. No information is given about toxicity to animals or therapeutic action. *L. P. Garrod*

Gentles, J. C., Barnes, M. J. & Fantes, K. H. **Presence of Griseofulvin in Hair of Guinea Pigs after Oral Administration.** [Correspondence.] *Nature*. 1959, Jan. 24, v. 183, 256–7.

Guineapigs were closely clipped, and given griseofulvin in oral doses of 30–40 mgm./kgm. daily for 23 days, meanwhile being housed individually on wire grids to prevent contamination of their fur by excreta. They were then clipped again and their hair was examined for the presence of the antibiotic. It was found to contain 5–6 μgm./gm., about one-half of which was removed by initial extraction with water, and was thought possibly to have been excreted by the skin and therefore merely adherent to the hair, the remainder being obtained by subsequent extraction with methanol. This fraction is believed to have been in the substance of the hair, and its presence would account for the effect of this antibiotic on infection by dermatophytes. The hair of untreated guineapigs yielded no activity. *L. P. Garrod*

Ito, F., Aoki, T., Yamamoto, M., Yuasa, M., Mizobata, H. & Tone, K. **The Mode of Action of Cycloserine (CS).** *Med. J. Osaka Univ.* 1958, Aug., v. 9, Nos. 1/2, 23–31, 3 figs.

This paper describes the results of a series of studies on the action of cycloserine on the vitamin B6 enzyme system, on the antagonism between cycloserine and α-alanine, and on the significance of metallic ions and their chelation with cycloserine.

Cycloserine inhibited the decarboxylation of glutamic acid by extracts of *Escherichia coli*, BCG, avian tubercle bacilli and mice brain extract; the inhibition ranged from 50–90% with 10^{-2}M cycloserine and 30–40% with 10^{-3}M concentration. The glutamic-aspartic transaminase of these same extracts was also inhibited to the extent of 65–90% by 10^{-2}M and 30–50% by 10^{-3}M cycloserine.

Because cycloserine inhibits the formation of indole by *E. coli*, attempts were made to determine the mechanism of the inhibitory action of cycloserine in the B6 enzyme system by means of the purified tryptophanase. The inhibitory action was found not to depend upon the duration that the antibiotic was in contact with apotryptophanase or other substrates but upon the duration that it was in contact with pyridoxal phosphate. The inactivation of pyridoxal phosphate could be explained by the formation of a Schiff's base, and in fact the authors claim that the formation of the base is easily demonstrable.

The chelating effects of cycloserine were examined by mixing 0·02 M cycloserine with 0·33 M $CuSO_4$ in veronal buffer. A yellowish green colour developed and the optimal *p*H was found to be around 7·0. The maximum colour was produced with a 2 : 1 ratio of the antibiotic to the salt, and the *p*H fell from 7·0 to 5·0. Also, when L-tryptophan and Cu++ were heated in a strong alkaline solution, the presence of cycloserine interfered with this non-enzymatic formation of indole. Cycloserine has an inhibitory effect on the spontaneous oxidation of adrenaline and ascorbic acid, and in experiments with ascorbic acid oxidase, cycloserine was shown to prevent the reactivation by Cu++ of the enzyme, inactivated by KCN. However, as the antibiotic had no influence on Cu++ already combined with the enzyme, the chelating affinity of cycloserine must be weak for metallic ions already combined with protein.

In the antagonism experiments, with a limited range of substances and H37Rv in Kirchner medium, only α-alanine showed a marked antagonistic effect; the range of substances included other amino-acids, fatty acids, purine- and pyrimidine-bases, nucleic acid, mono- and polysaccharides and vitamins. 25 μgm. per ml. DL-alanine reversed the activity of 125 μgm. per ml. cycloserine and a similar effect was observed with *Pseudomonas pyocyanea*, *Bacillus subtilis* and *E. coli* but the effective range of antagonism was small; L-alanine was slightly weaker than D- or DL-alanine. The antagonism was increased by the presence of pyridoxal and adenosine triphosphate but it was abolished by the presence of high concentrations of glycine. 10^{-2}M DL-alanine also reversed the inhibitory action of 10^{-2}M cycloserine on the formation of indole by *E. coli*.

The authors do not claim that these observations account for the antibacterial activity of this antibiotic, but they suggest that they are related to it.

S. R. M. Bushby

NUFFIELD PROVINCIAL HOSPITALS TRUST. **The Planning and Organization of Central Syringe Services.** 59 pp., numerous illustrations. 1957. London: Nuffield Lodge, Regent's Park, N.W.1. [2s. 6d.]

It is being increasingly accepted that the provision of a central service for the supply of sterile syringes is desirable not only on grounds of safety but also for administrative convenience. Boiling can no longer be accepted as a method of sterilization; STEWART [this *Bulletin*, 1957, v. 32, 476] has drawn attention to the difficulties of sterilizing syringes by autoclaving, DARMADY and Barrington BROCK have emphasized the unreliability of many hot-air ovens [*ibid.*, 1955, v. 30, 342] and DARMADY, HUGHES and TUKE [*ibid.*, 1958, v. 33, 262] have recommended the use of radiant heat conveyor-belt type of hot-air sterilizers. All this may confuse those who are anxious to start a syringe service. The Nuffield Trust's publication gives full and detailed advice on all aspects of initiating and maintaining such a service. There is information on the choice of accommodation, selection and training of staff and the choice of all items of equipment. This includes not only the syringes and needles but all items needed to clean, sterilize and pack them. There is a section on procedure both in the wards and the service department in which all processing techniques are fully described. In a useful discussion of costing, capital expenditure and running costs are analysed for services of various sizes.

In their introduction the authors state that their material is based on the actual experience of syringe services in a number of hospitals, and emphasize that their recommendations must be considered somewhat tentative, but no one who is responsible for running a syringe service or is considering doing so should neglect to study this valuable publication, which is packed with useful information not readily obtainable elsewhere.

J. C. Kelsey

NUFFIELD PROVINCIAL HOSPITALS TRUST. **Studies of Sterile Supply Arrangements for Hospitals. Present Sterilizing Practice in Six Hospitals.** 75 pp., numerous illustrations. [Refs. in footnotes.] 1958. London: Nuffield Lodge, Regent's Park, N.W.1. [5s.]

This report is part of a survey now being made of the requirements for hospital central sterile supply departments. Present methods were to be studied as a guide for future planning but the results were so disturbing that it was decided to publish them at once in a separate report. The 6 hospitals investigated ranged from a cottage hospital with 15 beds to a teaching hospital with 500; the locations of the hospitals and the ages of their buildings also varied widely. Attention was given mainly to wards, theatres and autoclaves.

In the wards attention is drawn to the location, design and equipment of clean utility rooms, to the lack of storage space and to a widespread vagueness about aseptic techniques. Boiling-type instrument and bowl "sterilizers" are criticized in detail as is the use of dressing drums which were frequently damaged, wrongly packed and incorrectly stored. The laying and use of dressing trolleys is discussed and also the disposal of dirty dressings and foul linen. Bedpan washers were generally inefficient.

The section on the operating theatres is shorter, and is concerned mainly with ventilation and matters considered in the section on wards.

The autoclaves were frequently badly sited. Of 17 autoclaves examined only 8 were considered to be functioning satisfactorily, but the commonest cause of failure was found to be bad operation. The operators were often conscientious but were seldom clear about their duties or to whom they were responsible. The routine control and testing of autoclaves were generally inadequate.

In addition to describing and commenting upon these matters the investigators examined swabs taken from various sites alleged to be sterile. Of 209 swabs taken from instruments, syringes and the inner surfaces of dishes and drums in wards and theatres no less than 36 (17%) proved to be unsterile.

In their final section of discussion and suggestions the authors conclude that immediate action is needed—(a) to improve the working of hospital autoclaves; (b) to introduce a substitute for hospital drums—they describe a cardboard box that they consider satisfactory; (c) to improve the technique for the sterilization of syringes—here they refer to the Nuffield report on the subject [see above]; (d) to raise the standard of routine practices: they suggest that each hospital should have a set of standard procedures for sterilizing worked out at sisters' periodical meetings and approved by the Control of Infections Committee of the hospital; (e) to better the disposal of dirty dressings, linen and bedpans. Most important of all they consider (f) the need to define responsibility for the efficient performance and control of all procedures they describe and criticize.

Useful information about methods used for testing autoclaves, the use of cardboard boxes instead of drums, the sterilizing of syringes and the design of disposable paper bags for dressings are given in appendices.

[For detailed information this report should be consulted in the original—an abstract can only give a partial idea of the ground covered by this timely and revealing document. It is somewhat variable in the depth of its coverage and some important topics are barely mentioned, but it is an interim report issued to draw immediate attention to pressing problems—future publications on this subject by the Nuffield Trust will be awaited with interest.] *J. C. Kelsey*

DARMADY, E. M., HUGHES, K. E. A., JONES, J. D. & VERDON, Patricia E. **Failure of Sterility in Hospital Ward Practice.** *Lancet.* 1959, Mar. 21, 622–4.

This paper reports on the bacterial standards of so-called sterile and disinfected articles in 7 British

hospitals. Instruments, bowls and dishes were examined by a swabbing technique. After boiling 21% of 169 instruments and 36% of 339 bowls and dishes were found to be contaminated, as were 26% of 133 Cheatle's forceps. The organisms found were mainly non-pathogenic. Of 248 positive cultures saprophytic staphylococci accounted for 54% and organisms of the "Subtilis group" for 35%. *Staphylococcus pyogenes* was, however, found in 2% and coliform organisms in 0·8% of instances. The authors comment that the boilers used were often inadequate in design or maintenance, that thermometers were not provided so that the only available criterion of ebullition was the unreliable one of turbulence, and that the duration of boiling was seldom accurately controlled. The great importance of cleaning instruments before boiling was not sufficiently understood.

Various chemical "sterilising" solutions were tested by immersing in them for 24 hours blades contaminated with *Clostridium tetani*. None were sterilized.

Samples of dressings from drums were cultured and 24% of 163 were found to be unsterile. This is associated with damaged drums, unsuitable storage conditions and the frequent opening of drums which may be in use over a period of several days.

It was observed that dressing trolleys were often prepared long before required, or a single trolley was used for a prolonged dressing round. On one occasion progressive contamination of a set of dishes laid up on a trolley was demonstrated over a period of 15 minutes.

Bedpans were swabbed for the presence of faecal organisms after various disinfecting processes. Sluicing alone yielded positive cultures on 100% of 93 occasions. Sluicing followed by boiling reduced this to 60% (11) of 18. Automatic apparatus in which washing was followed by steam injection gave better results, but even the best of the 3 tested showed 3 out of 12 positive cultures. Staphylococci were not isolated from heat-treated pans. The authors report that the BSI pattern of bedpan has an internally reflected seat which causes difficulty in sluicing, and the residual faecal matter is not disinfected by boiling. They consider that bedpan washer-sterilizers should have an automatically timed cycle, since with hand-operated apparatus enough time is seldom allowed.

In the general conclusion it is emphasized that much equipment is inadequate, and that those using it often do not understand the principles involved. It is concluded that in the long run the provision of central sterile supply services will prove the most economical and the safest arrangement.

[This paper is useful in providing yet more evidence that doubts about hospital sterilization are all too often justified. Direct sterility tests of the type described are, however, liable to a high rate of false positive results owing to chance contamination during sampling. This rate may be as high as 25% for dressings (SAVAGE, R. M., *Quart. J. Pharm. & Pharmacol*, 1940, v. 13, 237).]

J. C. Kelsey

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order: General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus; Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes, Leptospira; Anaerobes; Bacillus; Others.

CHOMICZEWSKI, J. Badania nad skojarzonym działaniem faga B i niektórych antybiotków na proces zmiany toksynotwórczości szczepów *Corynebacterium diphtheriae*. [**Studies on the Combined Action of Phage B and some Antibiotics on the Process of Changes in Toxigenicity of** *Corynebacterium diphtheriae*] *Med. Dosw. i Mikrob.* Warsaw. 1958, v. 10, No. 3, 297–307. [37 refs.] English summary.

A non-toxigenic strain of *Corynebacterium diphtheriae* was mixed with B phage and exposed to the action of antibiotics on agar plates, and the colonies growing around the zones of inhibition were examined for susceptibility to lysis and toxin formation. Organisms exposed to the action of penicillin and chlortetracycline remained sensitive to phage and did not form toxin. Strains exposed to chloramphenicol and oxytetracycline were not lysed by the phage and did not form toxin, and the same properties were found in a parallel experiment in which the initial strain was not mixed with phage before plating. *D. J. Bauer*

STRAUSS, N. & HENDEE, Edelmira D. **The Effect of Diphtheria Toxin on the Metabolism of HeLa Cells.** *J. Exper. Med.* 1959, Feb. 1, v. 109, No. 2, 145–63, 10 figs. [30 refs.]

The object of these investigations has been to get a more precise knowledge of the phase of cell metabolism which is blocked by the action of diphtheria toxin.

Working with growths of HeLa cells in a variety of special media the authors conclude that there is no serious interference with either glycolysis or O^2 uptake, since these continue little diminished after 4 hours' exposure when cell damage can already be determined by direct microscopic examination.

This study is extended by observations on the ability of the culture cells to take up methionine labelled with radio-active S isotope and evidence is presented in support of the conclusion that radio-activity demonstrated in cells filtered off from such cultures is in fact due to labelled methionine which has been incorporated in protein. These observations lead to the conclusion that protein synthesis is already checked 2 hours after exposure of the HeLa cells to toxin whereas the morphological evidence of cell damage appears first 2 hours later. Following up the observation of the close correlation of diphtheria toxin susceptibility and succinic dehydrogenase activity in the tissues of the silk worm embryo [PAPPENHEIMER & WILLIAMS, this *Bulletin*, 1952, v. 27, 969], the authors have compared the action of 2 inhibitors of that enzyme, cyanide and 2–4 dinitro phenol, with that of diphtheria toxin on the methionine uptake of HeLa cells.

These 2 substances are found to be more rapid but less complete in their action and when compared on the basis of the ratio of concentration to activity they appear to be much weaker than toxin, besides which they produce very little morphological change in the culture cells. At temperatures of 10°C. and below the HeLa cells do not take up toxin. *J. W. McLeod*

WOLF, B. & STAVITSKY, A. B. ***In Vitro* Production of Diphtheria Antitoxin by Tissues of Immunized Animals. II. Development of a Synthetic Medium which promotes Antibody Synthesis and the Incorporation of Radioactive Amino Acids into Antibody.** *J. Immunology.* 1958, Nov., v. 81, No. 5, 404–13. [41 refs.]

LUGOSI, L. **The Method of culturing *M. tuberculosis* with the Use of Freeze-Dried Loewenstein-Jensen Medium.** *Acta Tuberculosea Scandinavica.* 1959, v. 36, No. 4, 242–8. [12 refs.]

In Hungary during the last 10 years, the diagnostic cultural examinations for tubercle bacilli were carried out in the Central Diagnostic Laboratory, Budapest, but in order to improve the diagnostic work in regional institutions, laboratories were more recently organized in regional towns. Liquid medium is supplied in a concentrated form to these laboratories from the Central Laboratory, but difficulties are being encountered in supplying Löwenstein-Jensen medium and the possibilities of supplying it in a freeze-dried form have been investigated.

The completed medium, except for inspissation, was freeze-dried in 250 ml. amounts, and 14 days later reconstituted with distilled water. After standing for 1 hour at room temperature, it was distributed into tubes and inspissated.

The growth qualities of this medium were then compared with those of freshly prepared Löwenstein-Jensen medium and liquid modified Sula medium. This was done by comparing the rate and quantity of growth of inocula from dilutions, ranging from 10^{-6}–10^{-9}, of Dubos cultures of H37Rv, an isoniazid-resistant variant of this strain, and the Ravenel strain; 8 tubes of each of the media were inoculated with each of the dilutions.

The results, which were statistically analysed, showed that the freeze-dried medium was at least as good as the fresh medium, and the author claims that the freeze-dried material has the advantages that the medium can be prepared in mass when the season is most favourable for egg-supply, that production can be based on a poultry farm, and that the medium is more uniform.
S. R. M. Bushby

KATSUYAMA, S. & KANAI, K. **Application of "Agar Film Method" on Single Cell Culture of Tubercle Bacilli.** *Japanese J. Med. Sci. & Biol.* 1958, June, v. 11, No. 3, 109–16, 2 figs.

In a previous paper [this *Bulletin*, 1958, v. 33, 780], the authors described the use of the de Fonbrune pneumatic micromanipulator with a specially designed microforge attachment and phase contrast microscopy for single cell cultivation of *Escherichia coli*. In their present paper they describe the successful single cell culture of the tubercle bacillus.

Individual tubercle bacilli were obtained from a liquid Tween-albumin medium by means of a micropipette and placed on to small pieces of Kirchner medium on coverslips. The pieces of media were then placed on to slopes of the same medium and incubated for 4 weeks. When the bacilli were isolated from a satisfactory viable culture 60% or more of the bacilli developed into single colonies.

With this technique cultures of variants of H37Rv, resistant to isoniazid and to streptomycin, and of a streptomycin-dependent strain of tubercle bacilli, were shown to be heterogeneous by inoculating a number (4–12) of single bacilli from each on media containing varying concentrations of the drugs and by comparing the number of these bacilli which grew into colonies on the drug-containing media with those which grew on the drug-free medium.

The culture of H37Rv was shown to be heterogeneous for in a sensitivity test a few bacilli grew in 5 and 10 μgm. streptomycin per ml. but when similar tests were made on 15 single cell isolates from the culture no organism grew in concentrations greater than 1 μgm. per ml. There would therefore appear to be less heterogeneity in these daughter cell isolates than in the parent culture. *S. R. M. Bushby*

KATSUYAMA, S. & KANAI, K. **Dissociation of a Strain of Tubercle Bacilli by Single Cell Cultivation for Virulence Study.** *Japanese J. Med. Sci. & Biol.* 1958, June, v. 11, No. 3, 117–28, 8 figs. [14 refs.]

The method used for obtaining these single-cell isolates was the one described in the previous paper [see above], and the strain of tubercle bacilli used was the H2 human strain originally isolated in 1935.

The bacilli were grown in Dubos medium and 21 single cells were isolated but only 15 of these grew. Each of these isolates was inoculated into pairs of guineapigs and the 2 isolates which produced the maximum and minimum degrees of tuberculosis were subcultured 7 times and then 27 and 16 daughter isolates were taken, respectively, from each. These cultures were inoculated intravenously and subcutaneously into pairs of guineapigs and the degree of tuberculosis produced showed that the isolates from the culture of low virulence were not uniform, for 4 of the isolates showed moderate virulence, but those from the culture of high virulence were uniformly high.

From these daughter isolates, 1 was selected from the highly virulent line and 3 from the avirulent line, and these were subcultured and passaged 3 times in Dubos medium from which 4 bacilli were isolated from the virulent culture and 10 from each of the 3 avirulent cultures. When these bacilli had grown into colonies they were inoculated into guineapigs and the lesions produced confirmed that the cultures were now homogeneous. *S. R. M. Bushby*

ROYAL NETHERLANDS TUBERCULOSIS ASS. **Tubercle Bacilli and Pyruvic Acid** [STONEBRINK, B.]. *Proc. Tuberculosis Res. Counc.* 1957, No. 44, 67–74, 2 figs. on 2 pls. [18 refs.]

In this paper the author discusses the importance of pyruvic acid in the metabolism of the tubercle bacillus.

Human tubercle bacilli can use glycerol, glucose pyruvate and acetate as a source of carbon but bovine strains can use only pyruvates and acetates unless they are adapted to using glucose and glycerol. In the splitting of glucose, a number of intermediary compounds are formed, some of which are dioxyacetone, glycerol, glyceric acid, glyceraldehyde, pyruvic acid, lactic acid, citric acid and acetaldehyde; pyruvic acid thus has a central place in this system.

Tubercle bacilli have been shown to die when suspended in 6% glycerol [this *Bulletin*, 1944, v. 19, 477, 478] and the author, postulating that a metabolite was the cause, examined some of the intermediates. Pyruvic acid was non-toxic but glyceraldehyde and dioxyacetone were very toxic, and glycerophosphoric acid, phosphoglyceric acid, glyceric acid and lactic acid were of intermediate toxicity. When phosphate was added to the pyruvate solution the tubercle bacilli grew and the lysogenic bovine tubercle bacilli grow in Long's medium when 0·1% pyruvate is added.

Hydrogen peroxide reacts *in vitro* with pyruvic acid to form acetic acid and carbon dioxide, but it reacts with neither glucose nor glycerol.

Pyruvic acid reacts with isoniazid to form a hydrazone and as isoniazid in man can cause a fall in blood pyruvate, the neurotoxicity of over-dosage could be due to hypopyruvataemia; this suggestion is supported by the observation that in animals the toxicity of isoniazid is lowered by the administration of pyruvic acid. Because of these findings, the drug streptotibine, a combination of streptomycin, isoniazid and pyruvic acid, was developed.

The author mentions various hypotheses of the mode of action of isoniazid against the tubercle bacillus and emphasizes that none is entirely satisfactory; he points out that pyruvic acid is one of the several substances that have improved the growth of the catalase-negative, isoniazid-resistant tubercle bacilli. Apparently the metabolism of pyruvic acid by bovine strains and catalase-negative human strains differs. The failure of bovine strains to utilize glucose or glycerol lies in the dehydrogenase system and pyruvate does not need dehydrogenating; these strains possess catalase so there is no need for pyruvic acid to split the hydrogen peroxide but the catalase-negative strains need pyruvic acid to restore catalase action.

Finally, the author claims that this expectation that his pyruvate medium, which was originally developed for the cultivation of bovine strains, would be valuable for the growth of isoniazid-resistant strains, is fulfilled. The formula of this, a coagulated egg-medium containing approximately 0·3% pyruvic acid, is given in an addendum.

S. R. M. Bushby

AOYAGI, T. & MIZUNO, D. **Chemical Nature of a Substance which was extracted from Egg Yolk and reported by Yamane to be Growth-Stimulatory to** *Mycobacterium tuberculosis*. *Japanese J. Med. Sci. & Biol.* 1958, Oct., v. 11, No. 5, 401–5, 4 figs.

"Therefore, it can be concluded that the substance isolated and crystallized from egg yolk and reported by Yamane (1957) to be growth-stimulatory to *Mycobacterium tuberculosis* is a triglyceride fatty acids of which can be varied depending on the preparation. Other substances contaminated in the preparation, *e.g.* a steroid, is not presumed to play a main role in a growth culture, since its yield was so small (1%)."

[See this *Bulletin*, 1957, v. 32, 697, 896.]

HIRSCH, A. & CATTANEO, C. I micobatteri: costituzione chimica e virulenza. II.—Il potenziale di ossido-riduzione dei micobatteri. [**The Mycobacteria, their Chemical Composition and Virulence II. Oxidation-Reduction Potential of Mycobacteria**] *Giorn. di Microbiol.* Naples. 1957, Nov.–Dec., v. 4, No. 3, 175–92, 2 figs. [26 refs.] English summary.

In addition to a considerable discussion of the existing observations on this subject, the divergent results which have been obtained and the obvious difficulties of such observations, the authors' own results are recorded. Direct potentiometric observations have not given sufficiently constant results to be made the basis of conclusions. The results obtained with indicator dyes are, however, fully recorded.

16 different dyes were tried out but 6 of these had to be rejected because they were too strongly absorbed by the bacteria and the solution was decolorized independently of reduction of the dye.

Finally, the series phenol-indophenol (+ 223 mV), 2 : 6 dichlorophenol indophenol (+ 217 mV), toluylene blue (+ 104 mV), thionine (+ 62 mV) and indigo tetrasulphonate (− 30 mV) were chosen as presenting a gradation of potentials at their reversal points suitable for covering the range required by mycobacteria.

5 mgm. of a freshly grown culture in Sauton synthetic medium were suspended in 0·02 or 0·05% solution of the indicator in buffer at *p*H 7·0 and reduction or absence of reduction read after 30 minutes at room temperature.

A control series of observations was made with 2 : 6 dichlorophenol indophenol made up in graded Sorensen phosphate buffer solutions from *p*H 5·0 to *p*H 9·0 so that the potential, varying by 60 mV with each *p*H degree, gave a scale + 366 mV to +89 mV.

The two methods gave closely corresponding results with a collection of 59 strains of which 42 were stock strains and 17 had been recently isolated. The human and bovine pathogenic strains failed to reduce substances of potential more negative than + 217 mV whereas the avian strains usually reduced substances with potential level of + 104 mV and the saprophytic strains usually reduced even at + 62 mV levels. The BCG strain fell into the group of pathogenic strains.

[For Part I, see this *Bulletin*, 1958, v. 33, 1080.]

J. W. McLeod

RIBI, E., PERRINE, T., LIST, R., BROWN, W. & GOODE, G. **Use of Pressure Cell to prepare Cell Walls from Mycobacteria.** *Proc. Soc. Exper. Biol. & Med.* 1959, Mar., v. 100, No. 3, 647–9, 2 figs.

SAENZ, A., Jr. La tuberculose expérimentale du hamster doré. [**Experimental Tuberculosis of the Golden Hamster**] *Ann. Inst. Pasteur.* 1958, Nov. & Dec., v. 95, Nos. 5 & 6, 534–56, 11 figs. [29 refs.]; 694–720, 10 figs. [27 refs.]

This article is an extensive and detailed description of the lesions produced in the golden hamster by the injection of virulent isoniazid-sensitive strains of bovine, human and avian tubercle bacilli and human strains resistant to isoniazid; both the macroscopic and the microscopic appearances of the lesions are described.

The first part of the article deals with the lesions produced by doses of the isoniazid-sensitive bovine and human strains, ranging from 10^{-5} to 1 mgm., injected intraperitoneally and subcutaneously.

With the bovine strains (Ravenel-Nouff, Dupray S and 1033) the survival time of the animals ranged from 22 to 182 days, the time depending upon the strain, the size of the infecting dose and the route, but the H37Rv human strain was much less virulent for the average survival time ranged from 76 to 164 days. The survival times with both types of tubercle bacilli were shorter when the organisms were injected intraperitoneally than when given subcutaneously but with the human strain the disease was limited mainly to the lungs and spleen. The bovine strain lesions were much more widespread and caseating.

The second part of the article describes the effects produced by the isoniazid-resistant strains. 3 of the strains (689A, 659A and DEM), in doses ranging from 10^{-3} to 1 mgm., killed the hamsters in 72 to 220 days and lesions were found in the glands and the viscera, especially the lungs and the grossly enlarged spleens; the glands were caseous. 1 of these strains was resistant to 1 μgm. isoniazid per ml. and was catalase-negative, the others were catalase-positive and resistant to 0·2 and 0·5 μgm. per ml. respectively. Another of the strains (607A) was resistant to 5 μgm. per ml. and was catalase-positive; the fifth strain (111E) was resistant to 1 μgm. per ml. but was catalase-negative. Neither of these latter strains, with doses of 10^{-3} to 1 mgm., killed the hamsters although 1 of the animals was killed after 10 days and another after 40 days; the other animals were killed from the 120th to the 425th day. Doses of 10 mgm., however, caused death within 227 and 353 days. The lesions produced by the 2 strains were minimal and regressive and were present in the liver, spleen, lungs and distal glands.

The last experiments were with *Mycobacterium avium*, strain 17, and with doses of 10^{-2} to 10 mgm. no deaths occurred during the observation period of 120 to 395 days. There was little or no evidence of tuberculosis and the bacilli were rapidly eliminated except from the glands.

The author discusses the histological changes at some length and concludes that the changes are similar to those observed in man treated with isoniazid, and that an especial feature of the disease in these animals is the lymphatic spread. The general conclusions are that the hamster is intermediate between the mouse and the guineapig in response to infection with isoniazid-resistant strains and that it is probably of special value in differentiating the human and bovine strains.

S. R. M. Bushby

JANICKI, B. W. **Circulating Levels of the "Plasma Factor" responsible for *in vitro* Leukocyte Cytolysis during Sensitization of Guinea Pigs with *Mycobacterium tuberculosis*.** *Amer. Rev. Tuberculosis.* 1959, Feb., v. 79, No. 2, 244–5.

Leucocytes from a tuberculin sensitive host are lysed *in vitro* by tuberculin (*Proc. Soc. Exper. Biol and Med.*, 1947, v. 65, 269) but not if they are first washed in saline. Experiments with normal cells showed that they too would lyse if they were suspended in tuberculous plasma and exposed to tuberculin, an observation which led to the conception of "plasma-factor" [this *Bulletin*, 1949, v. 24, 852]. In the present experiments guineapigs were immunized with dead H37Rv and the rate of development of this plasma factor was followed.

The test for the presence of the factor was done within 4 hours of bleeding the animals because of the lability of the factor, and it consisted of placing 0·1 ml. of normal leucocytes, obtained from the buffy coat of heparinized blood, and 0·3 ml. of test serum into a siliconized tube, and then adding 0·1 ml. of saline containing 5 μgm. PPD. A control tube without the PPD was also set up and the leucocytes present in both tubes were counted after rotation at 5 r.p.m. for 2 hours at 37°C. The cutaneous tuberculin reactions of the animals were also followed.

The results showed that the factor was definitely detectable by the 5th day, reaching a peak concentration during the 7th–12th days and then absent by the 17th day. The tuberculin reaction was weakly positive on the 7th day and continued to increase until the 17th day.

This earlier development of the plasma factor as compared with skin hypersensitivity is considered of especial interest in view of the fact that leucocytic hypersensitivity has also been shown to develop earlier than skin hypersensitivity [*ibid.*, 1958, v. 33 (271), *Amer. Rev. Tuberculosis*, 1957, v. 76, 888].

S. R. M. Bushby

HALL, C. H., Jr. & ATKINS, E. **Studies on Tuberculin Fever. I. The Mechanism of Fever in Tuberculin Hypersensitivity.** *J. Exper. Med.* 1959, Apr. 1, v. 109, No. 4, 339–59, 10 figs. [37 refs.]

WECHSELBERG, K. Über die Wirkung ätherischer Öle auf das Wachstum von Tuberkelbakterien *in vitro*. [**The Effect of Volatile Oils on the Growth of Tubercle Bacilli** *in vitro*] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 2, 166–80. [Numerous refs.]

The author investigated the inhibitory effect of various volatile oils on the growth of tubercle strains, including H37Rv and also recently isolated strains from tuberculous patients. 2 test methods were used, *viz.* (i) exposure of inoculated egg slopes during incubation to the vapour of the volatile oil concerned, and (ii) the incorporation of different concentrations of oil in cultures in Kirchner medium. Considerable activity was shown by some of the volatile oils tested. Thus, the growth of inverted cultures of tubercle bacilli in 50 ml. containers was completely inhibited when 0·02 ml. of

aniseed, peppermint, cinnamon or fennel oil was added to the cotton wool plug of the culture before the container was made air-tight with a paraffin seal. Subcultures from the exposed slopes on to fresh media after 4 weeks' incubation remained sterile.

In Kirchner medium, the most active oils in preventing growth of tubercle bacilli, and the corresponding inhibitory concentrations, were oil of cinnamon (1 in 20,000), peppermint oil (1 in 6,666), ol. caryophylli (1 in 6,666), oil of lavender (1 in 4,000) and oil of bergamot (1 in 4,000). *B. Moore*

SERI, I. **A Clinical Evaluation of the Factors involved in the Resistance of Tubercle Bacilli to Antituberculous Drugs.** *Acta Tuberculosea Scandinavica.* 1959, v. 36, No. 4, 277–88, 1 fig. [24 refs.]

Several authors have already investigated certain factors that influence the development of resistance, but the purpose of the present study was to investigate some of the less known factors.

From the evaluation of the clinical and laboratory data of 381 patients, 105 with cavitary disease, positive sputum and prolonged stay in hospital, were selected for this study. During the period of observation, 1,179 resistance tests were performed for isoniazid, 1,190 for streptomycin and 1,040 tests for PAS, making an average of 33 tests per patient. Indirect tests in liquid medium were used. 90 of the patients were treated with double combinations of the drugs and 15 received the triple combination.

Changes in the resistance of bacilli were correlated, (1) with transient stress in the patient as from influenza, bronchography, thoracoplasty and the side-effects of drugs, (2) with evacuation of excavated caseous infiltrations, (3) changes in the tuberculous process during continuous chemotherapy, and (4) with prolonged but unsuccessful chemotherapy followed by the institution of a "new" drug.

The author concludes from this study that in patients on chemotherapy, changes in the pulmonary lesions or in the defensive state of the body are invariably followed by changes in the drug-resistance of the bacilli. Lowering of the body defences, stagnation or worsening of the pulmonary lesions lead to increase in drug-resistance, whereas an improvement in the lesions leads to retardation in the development or to a lessening of resistance. From these facts it follows that patients with cavitary disease and positive sputum should be protected from stresses during chemotherapy, and that every attempt should be made to maintain improvement, even by using drugs of secondary importance, *e.g.* pyrazinamide, viomycin and the thiosemicarbazones. A failure to realize these factors may result in prolonged treatment with the same drugs and thus produce an increase in the level of drug-resistance without a beneficial effect. *S. R. M. Bushby*

ROYAL NETHERLANDS TUBERCULOSIS ASS. **Resistance and Virulence of Tubercle Bacilli. A. Resistance in Sanatorium Cases** [KRAAN, J. K.], 34–42. **B. Resistance, Catalase-Activity and Virulence of Tubercle Bacilli in the Laboratory** [VAN DIJK, B.], 43–50, 2 figs. [11 refs.] **C. The Clinical Significance of the Loss of Virulence of Isoniazid-Resistant Tubercle Bacilli** [MULDER, R. J.], 51–61. **D. Viability and Virulence of Tubercle Bacilli found in Resected Tuberculous Pulmonary Tissue. Preliminary Remarks** [MULDER-DE JONG, M. T.], 62–6. *Proc. Tuberculosis Res. Counc.* 1957, No. 44, 34–66.

These papers come from the Beatrix-Oord Sanatorium, Appelscha, the Netherlands, and the first of them reports the increase in frequency of strains of tubercle resistant to streptomycin, PAS or isoniazid in the patients during 1952 to 1957. During this period, 2,032 positive cultures were examined for resistance and 764 cultures from 152 patients yielded bacilli resistant to one or more of the drugs.

	No. of cases with resistance to:—							
Period	PAS	SM	INH	PAS + SM	PAS + INH	SM + INH	SM + INH + PAS	Total
1952–53	15	6	11	6	13	3	33	87
1954–55	5	1	12	1	6	2	8	35
1956–57	2	1	10	2	4	2	9	30

The number of patients with bacilli resistant to streptomycin was already much lower in 1952–3 than in the previous years when streptomycin was used alone, but the number of patients with bacilli resistant to all 3 drugs was high and this was attributed to treatment either with the drugs separately or inadequately when given together; the prognosis in these patients was poor and 9 died and 20 were treated surgically.

In 1954–5 the incidence of isoniazid resistance predominated, a state that was attributed to treatment with the drug alone or to inadequate combined therapy and in 1956–7 this predominance became even more definite; 8% of the patients admitted to the sanatorium during this latter period had isoniazid-resistant strains. The high incidence of isoniazid-resistance can be partly explained by the fact that the drug is willingly taken by the patient whereas PAS is often refused.

In discussing these results the author expresses the opinion that in spite of there being some evidence that the encouragement of resistance to isoniazid is beneficial because of the often concomittant decrease in virulence, drug-resistance should be prevented if possible.

Since 1952, the catalase-activity and the virulence of the isoniazid-resistant strains have been studied by the second author, and the second paper summarizes the results. The catalase-activity was measured by the amount of bubbling that took place when H_2O_2 was added to the culture and the virulence was judged by the extent of tuberculosis present 3 months after injecting 0·2 mgm. of bacilli subcutaneously into guineapigs.

Of 50 strains resistant to 1 μgm. or more isoniazid per ml. and tested for virulence from the growth on the control tube containing no drug, 3 of the 6 catalase-positive strains showed decreased virulence whereas of the 44 catalase-negative strains, only 3 were highly virulent. However, when the virulence test was made on 33 of these strains, by using the growth from the

tube containing 1 μgm. isoniazid per ml., all showed decreased virulence and only 1 of these was catalase-positive.

From the results of these and other tests, the author reached the following conclusions: normally sensitive and heterogeneously low resistant populations show catalase activity and are usually of normal virulence for the guineapig, and bacilli resistant to 1 μgm. per ml. are usually catalase-negative and of low virulence.

The author of the third paper endeavoured to determine the clinical significance of changes in virulence of the strains isolated from the patients during 1955 onwards. The data are from 150 tests made on strains from 30 patients, who are divided into 3 groups. The first group consists of 12 patients in whom bed rest and chemotherapy, including isoniazid, brought about cavity closure and lasting sputum conversion. The bacilli from 10 of the patients were of normal or slightly decreased virulence and catalase activity, and their resistance to isoniazid ranged from 0·3 to 1·0 μgm. per ml. The bacilli from the other 2 patients were resistant to 10 μgm. isoniazid per ml. although their virulence was unusually high for resistant strains. The second group consisted of 13 patients in whom the cavities remained open and their sputa did not convert in spite of prolonged chemotherapy; these patients were apyrexial and in a stable state. The cultures from most of these patients were attenuated and resistant to 1–10 μgm. isoniazid per ml. Resections were done on 6 of the patients and thoracoplasty on 1 other; isoniazid is being given to 3 of the other patients with the object of suppressing the catalase-positive, virulent part of their bacillary populations. The third group consists of 2 patients who had died from progressive tuberculosis and 3 from other causes. The bacilli from one of the former patients were highly virulent but those from the other were attenuated. The tuberculosis of the latter 3 patients was in a stable state and the bacilli were attenuated.

The unfavourable signs observed in the 13 cases that were considered to be in a stable state were: (1) increased cavitation in 2 patients with attenuated strains and 2 with virulent strains; (2) dissemination in 1 patient with an attenuated strain, and possibly in 2 with virulent strains; (3) a poor general condition necessitating re-admission to the sanatorium in 1 patient with attenuated bacilli and in 2 others with virulent strains; and (4) an increase in virulence occurred in 1 patient with an attenuated strain and in 2 others with virulent strains (this change is considered a serious sign).

The results in these 30 patients can be summarized:—

Virulence	No. of patients	Recovered with bed rest and chemotherapy	Remaining positive with open cavities	Died
Low	14	3	9	(2)*
Moderate	6	1	4	(1)*
High	10	8	0	2

*Died from a non-tuberculous disease.

The author of the fourth paper gives a preliminary report on the viability and virulence of bacilli from resected lungs. He states [the evidence is to be published elsewhere] that the conclusions are the same as those of STEWART *et al.* [this *Bulletin*, 1957, v. 32, 566] *i.e.* that there is correlation between viability and the duration of chemotherapy in patients with drug-sensitive organisms, but not in patients with drug-resistant organisms. In this paper the author, however, also describes virulence tests made in hamsters.

The mean survival time of these animals after the inoculation of 0·05 mgm. of isoniazid-sensitive strains of tubercle bacilli was 2 months, but the animals usually survived 8 months when inoculated with isoniazid-resistant strains. Experience with 6 resistant strains from resected lungs showed: (1) that isoniazid-sensitive bacilli can often be recovered from apparently homogeneously resistant cultures by serial passage in this animal; (2) that the loss of virulence of isoniazid-resistant strains in this animal is graduated; and (3) that strains resistant to 30 μgm. isoniazid per ml. show considerable attenuation. *S. R. M. Bushby*

TSUKAMURA, M., NODA, Y., YAMAMOTO, M. & HAYASHI, M. **Genetic Considerations of the Mechanisms involved in PAS-Resistant Tubercle Bacilli.** *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 371–3.

ANDREJEW, A., GERNEZ-RIEUX, C. & TACQUET, A. Action de l'INH et de la D-cyclosérine sur la peroxydase purifiée et sur l'activité peroxydasique des bacilles tuberculeux. [**Action of Isoniazid Hydrazid and D-Cycloserine on Purified Peroxidase and Peroxidase Activity of Tubercle Bacilli**] *Ann. Inst. Pasteur.* 1959, Feb., v. 96, No. 2, 145–63, 4 figs. [25 refs.]

The peroxidase used in this study was from horseradish and the effects on its activity were determined by the decreased oxidation of guaiacol or pyrogallol in the presence of hydrogen peroxide, the decrease being measured colorimetrically.

Isoniazid in a concentration of $3{\cdot}65 \times 10^{-3}$M and D-cycloserine in a concentration of 78×10^{-3}M had an inhibitory effect on the activity of this enzyme, but no additive effect was observed when the 2 drugs were acting together. Isonicotinic acid had no inhibitory action on this enzyme or on the growth of tubercle bacilli, but hydrazine (NH_2NH_2) and sodium azide were both powerful inhibitors of peroxidase, their activity being greater than that of isoniazid although their inhibitory effect on the tubercle bacillus is much weaker than that of isoniazid. Serine had no anti-peroxidase activity.

Measurement of the peroxidase and catalase activities of the H37Rv, H37Ra, BCG and Ravenel strains of tubercle bacilli, and of their isoniazid and D-cycloserine resistant variants, showed that whereas the isoniazid-resistant variants are both catalase- and peroxidase-negative, the cycloserine-resistant variants may show a slight reduction in peroxidase activity but their catalase-activity is usually higher than that of the parent strain.

The catalase and peroxidase activity of 13 saprophytic mycobacteria was also studied, and in general their activities were similar to those of tubercle bacilli but their highly isoniazid-resistant variants showed reduced catalase activity and little or no peroxidase activity. *S. R. M. Bushby*

TAKAHASHI, Y. & NAGAYAMA, Y. Sur le mécanisme de développement non sélectif de l'isoniazido-résistance du *Mycobacterium tuberculosis*. **[On the Non-Selective Mechanism of the Development of Isoniazid Resistance by *Mycobacterium tuberculosis*]** *C.R. Soc. Biol.* 1958, v. 152, Nos. 8/9, 1290–92, 2 figs.

Bacteria are considered to become resistant to antibacterial drugs either by selection, induction or adaptation. In an experiment described in this paper, the authors consider that they have shown that tubercle bacilli can become resistant to isoniazid by induction.

A virulent strain of tubercle bacilli, H_2, was grown for 10 days in tubes of Dubos medium and then isoniazid, 10 μgm. per ml. was added to half of the tubes. 1 set of these tubes and 1 of the control tubes without isoniazid were incubated for 8 weeks in carbon dioxide and the other set of tubes were incubated for the same period in air. At various intervals the total number of bacilli present in each culture was determined turbidometrically, the number of living bacilli by viable counts, and the number of resistant variants by making viable counts on media containing 5 μgm. isoniazid per ml.

The counts made from the isoniazid-containing medium grown in air showed that although the number of bacilli revealed by the total and viable counts remained almost constant, the proportion of bacilli resistant to isoniazid increased until by the 6th week almost all the bacilli were resistant. No resistant bacilli developed in the cultures incubated in carbon dioxide. Examination of the cultures by electron microscopy showed no evidence of lysis and so in the absence of evidence of multiplication these bacilli had developed resistance, a condition which excludes the possibility that the change had been due to selection.

S. R. M. Bushby

MUFTIC, M. K. **Investigation of Resistance of Mycobacteria to Decolorization.** *Tubercle.* 1959, Feb., v. 40, No. 1, 50–53.

In this investigation, smears of H37Rv were stained by the Ziehl-Neelsen technique (ZN) and by the trimethinquino-cyanin technique (TMC), and the attempts to remove the factor responsible for the "decolorization resistance" were made by immersing suspensions of the bacilli in certain detergents. These detergents were known to have a pronounced defatting action and a special blending action on free fatty acids. They readily remove free fatty acids which may be present in the outer layers of the mycobacterial cell wall, and in an attempt to prevent other lipid fractions being removed from the bacilli they were also used half-saturated with sodium chloride. After immersion for varying periods in the detergents, the bacilli were washed with one of the alcohols or glycerols, and smeared on to slides and stained.

10 different detergents were used and the results show that whereas 1–6 hours' exposure resulted in the loss of resistance to decolorization in the ZN method, more than 10 hours' exposure was necessary before the bacilli failed to retain the TMC stain. The salted detergents prolonged only slightly the exposure period necessary to affect the ZN stain, but markedly lengthened the period necessary to affect the other stain, for even after the maximum exposure time of 48 hours 8 of the detergents had not affected decolorization. These findings suggest that the mechanism of staining by the 2 methods differs in some respect, and this conclusion was supported by the observation that treatment with chromic acid caused loss of the "decolorization resistance" by the ZN technique after 4 hours' exposure but by the TMC method only after 10 hours' exposure.

Ability to resist the decolorization in the ZN stain was restored by immersing the bacilli in ether solutions of alpha- or beta-3-hydroxy-x-methoxymycolanoic acid, provided the exposure to detergents was not prolonged until resistance to the decolorization with the TMC stain was lost.

The author interprets these results as indicating that resistance to decolorization in the ZN method depends on the presence of free mycolic acids, and on other lipids (non-fatty acids) in the TMC method, and as resistance to decolorization cannot be restored by immersion in mycolic acid when these other lipids are lost, the mycolic acids are fixed to the cells by these other lipids.

S. R. M. Bushby

BERTHRONG, M. & HAMILTON, Mary A. **Tissue Culture Studies on Resistance in Tuberculosis. II. Monocytes from Normal and Immunized Guinea Pigs infected with Virulent Human Tubercle Bacilli.** *Amer. Rev. Tuberculosis.* 1959, Feb., v. 79, No. 2, 221–31, 6 figs. [11 refs.]

On account of conflicting evidence for the existence of differences in the ability of monocytes from immunized animals and unimmunized animals to inhibit the multiplication of tubercle bacilli [this *Bulletin*, 1953, v. 28, 659; 1954, v. 29, 871], the authors have re-examined the problem. In their experiments, the monocytes were obtained from the peritoneal cavity of guineapigs, injected 1 week earlier with 1 ml. of mineral oil and the procedures used for infecting the cells with tubercle bacilli and of culturing the cells were those previously described [*ibid.*, 1958, v. 33, 879], extracellular multiplication of the bacilli being prevented by adding 5 μgm. streptomycin per ml. to the culture fluid. The guineapigs were immunized with BCG or by inhalation of a catalase-negative strain of tubercle bacilli.

In repeated experiments no difference was detected in the rate of phagocytosis by the immune or non-immune cells, or in the lethal effect of the tubercle bacilli on the 2 types of cells—in fact, with a heavy infection there may have been higher mortality in the immune cells during the first 48 hours. The onset of migration from the clot can be regarded as evidence that the cells have recovered from the trauma received during their preparation, and this occurred as rapidly with the non-immune cells as with the immune ones.

A slight difference was detected in the proportion of cells containing 1–5, 6–10 or 11–20 bacilli per cell, suggesting that the bacilli multiplied less rapidly in the immune cells and this became more definite when

the presence of "cording" of the bacilli within the cells was taken as evidence of multiplication; the inhibition was, however, only relative to the control cells and was not absolute. The use of "cording" as the criterion for multiplication enabled the increase in the numbers of intracellular bacilli due to phagocytosis of bacilli from dead cells to be readily distinguished from multiplication of the originally phagocytosed bacilli.

S. R. M. Bushby

LURIE, M. B., ZAPPASODI, P., LEVY, R. S. & BLAKER, R. G. **On the Role of the Thyroid in Native Resistance to Tuberculosis. I. The Effect of Hyperthyroidism.** *Amer. Rev. Tuberculosis.* 1959, Feb., v. 79, No. 2 152–79, 6 text figs. & 14 figs. on 4 pls. [16 refs.]

There is evidence which suggests that the underlying mechanisms of resistance to infectious diseases in general share certain dominant factors which may be influenced by hormones. For example, pharmacological doses of cortisone can lessen the innate capacity of monocytes from resistant animals to inhibit the growth of tubercle bacilli [this *Bulletin*, 1951, v. 26, 869] and apparently it is this resistance which plays an important role in natural resistance, enabling the infection to be held in check until acquired resistance develops. There is also evidence that acquired resistance to tuberculosis is associated with a non-specific increase in the physiological activity of the monocytes, and since thyroid hormones increase the metabolism of cells and accelerate their growth and differentiation, the authors have determined the effects of hyperthyroidism on the natural resistance of rabbits to tuberculosis.

The rabbits used in these experiments were of 8 strains of different genetical resistance and a state of hyperthyroidism was induced by the administration of L-tri-iodothyronine or L-thyroxine, its extent being measured by the oxygen consumption of the rabbits. The resistance to tuberculosis was assessed by determining the number of tubercles that developed in the lungs, after a single inhalation of H37Rv, the size of the tubercles and the extent of caseation; the effects of the hyperthyroidism were assessed also by quantitative cultures of the lungs, lymph nodes and spleen. The allergic state and non-specific irritability were compared by relating the intensity of tuberculin reaction to the inflammatory response produced by the intracutaneous injection of indian ink or turpentine. Approximately 350 rabbits were used in these experiments.

In infected rabbits of intermediate native resistance no change was observed in oxygen consumption during the infection, but when 40 μgm. of tri-iodothyronine was administered either daily or on alternate days before and after infection, the oxygen consumption increased by 30% or more and the animals lost more weight than the control animals, thus confirming that the animals were in a hyperthyroid state.

Analysis of the results of the infection in the hyperthyroid animals showed that the inception and the progress of the disease were suppressed to a greater or lesser degree in rabbits of intermediate or moderately low natural resistance. Calculated from the decrease in the number of tubercles in the lungs, this increase in resistance was estimated as being from 4 to 20 times, which raised the resistance to that of the highly resistant strain; hyperthyroidism had little or no effect on a strain of rabbits of very low resistance or on one of very high resistance. Natural resistance apparently operates by inhibiting the accumulation of bacilli in the lungs and these hormones apparently act by increasing this inhibition; the increase ranged from 10- to 40-fold in the tri-iodothyronine and 3- to 10-fold in the thyroxine-treated animals as compared with the number of bacilli in the lungs of untreated animals.

The effects of treatment were, however, not confined to enhancing natural resistance; the progress of the lesions was also modified even when treatment was delayed for 21 days. These effects were shown by a decrease in the size of the tubercles, a marked suppression of caseation, an accentuation of interstitial inflammation, and by the tubercle bacilli being scanty, short, poorly stained and rarely showing cording. Resolution of the tubercles was also frequently more advanced in the treated animals. All these changes are essentially expressions of restricted multiplication of the bacilli, but the hormones have no activity *in vitro* against the tubercle bacillus. The reduction in bacillary multiplication reduced the tuberculin sensitivity but hyperthyroidism itself had no effect on the reaction.

High native resistance, contrary to expectation, enhances the spread of the bacilli to the lymph nodes and a similar effect was observed in the hyperthyroid animals, although it was greater with tri-iodothyronine than with thyroxine treatment. *S. R. M. Bushby*

LURIE, M. B., ZAPPASODI, P., BLAKER, R. G. & LEVY, R. S. **On the Role of the Thyroid in Native Resistance to Tuberculosis. II. The Effect of Hypothyroidism. The Mode of Action of Thyroid Hormones.** *Amer. Rev. Tuberculosis.* 1959, Feb., v. 79, No. 2, 180–203, 11 figs. (4 coloured) on 3 pls. [25 refs.]

This paper is complementary to the preceding paper [above] for it shows that hypothyroidism reduces natural resistance. The hypothyroid state was induced by thyroidectomy or by administering propylthiouracil, and the infection was produced by inhalation of H37Rv.

In contrast to the effects of hyperthyroidism, hypothyroidism was shown to increase the number of tubercles in the lungs, to intensify the progress of the disease and to accelerate caseation. These effects were less pronounced with the propylthiouracil treatment than by thyroidectomy and in many ways the effect of the removal of the thyroid resembled those of treatment with cortisone—both depressing perifocal inflammation, tuberculin sensitivity and antibody production; these effects on antibody production were measured by the response to stimulus with bovine albumin as the antigen. Hyperthyroidism increased the response to this antigen.

The role of the thyroid state in tuberculosis is discussed at some length, but the authors are unable to account for the suppression of bacillary multiplication in the hyperthyroid state or for thyroidectomy decreasing resistance. They emphasize that a mere increase in metabolic state does not increase resistance, for in rabbits treated with dinitrophenol, resistance was

decreased in spite of this substance being calorigenic. That hyperthyroidism increases cellular activity is suggested by the increase in antibody production observed in this state as compared with the lowered production of the hypothyroid state, in which there is atrophy of the lymphoid tissue. However, the various host-parasite relationships, observed in these experiments with differing thyroid states, unquestionably support the hypothesis that thyroid function is one of the constitutional factors controlling natural resistance to tuberculosis in rabbits.

S. R. M. Bushby

KIKUTH, W. & POTHMANN, F. J. Zur Kombination von INH-Prophylaxe und BCG-Schutzimpfung. [**Combined Use of Isoniazid and BCG in the Prophylaxis of Tuberculosis**] *Deut. med. Woch.* 1959, Feb. 20, v. 84, No. 8, 360–64, 407. [25 refs.]

Vaccination with an isoniazid-resistant strain of BCG combined with the administration of isoniazid has been advocated on the grounds that this procedure will ensure both immediate and delayed protection against virulent infection. The theory on which it is based is that isoniazid will prevent dissemination of a primary infection contracted before the development of post-vaccinal immunity and that the use of a resistant strain of BCG will permit the organisms of the vaccine to multiply without inhibition by the isoniazid.

The authors carried out experiments on guineapigs to test the above theory. In addition to 22 control animals 7 groups of a total number of 108 were used. All were non-reactors to tuberculin. Groups 1–3 were vaccinated with isoniazid-resistant BCG, groups 4–6 with normal BCG, group 7 with heat-killed BCG and the controls were left unvaccinated.

On the day after vaccination the animals in groups 1 and 4 began to be given isoniazid, 1 mgm./100 gm. 6 times weekly, those in groups 2 and 5 received 2 mgm./100 gm. twice weekly, and those in groups 3 and 6 and the controls did not receive isoniazid.

One day after the end of treatment with isoniazid the vaccinated animals were tested with tuberculin (OT 1/5) and 3 days later infected with *Mycobacterium tuberculosis* H37Rv.

After the challenge infection all animals in the experiment were left for 3 months without further treatment, after which time all but one in each group were killed and examined. Macroscopic, microscopic and bacteriological examination of tissues was made and a quantitative estimation of the disease present made. The survival time of the solitary animal left in each group was recorded.

The results were:

Groups	1	2	3	4	5	6	7	Controls
Vaccine	R	R	R	N	N	N	K	–
Isoniazid	C	I	–	C	I	–	–	–
Post-vacc. Allergy	++	++	++/+++	+/++	++	++	++	–
Number	16	16	12	16	16	11	21	22
Index of Disease	1·28	0·86	1·04	2·19	1·46	1·07	4·05	9·14

R = Resistant, N = Normal, C = Continuous, I = Intermittent, K = Killed.

The immunizing power of the resistant vaccine was seen to differ little from that of normal vaccine (indices 1·04 and 1·07 respectively).

Comparison of groups 1–2 and 4–5 vaccinated with resistant and normal vaccine respectively showed that better protection was afforded when isoniazid was given intermittently than when it was given continuously.

The difference is seen especially in groups 4 and 5 in both of which normal vaccine was used. The advantage of intermittent isoniazid is that it gives normal BCG a better chance to multiply and so produce a greater degree of immunity.

The authors emphasize that the above findings are those found in experimental animals and they cannot be applied to man without further experiment.

H. G. Calwell

ZAPF, K. Vergleichende Untersuchungen zur Morphologie und Zytologie des Mycobakterium tuberculosis (BCG). II. Mitteilung. Licht- und elektronenmikroskopische Befunde zum Kernproblem. [**Comparative Investigations on the Morphology and Cytology of *Mycobacterium tuberculosis* (BCG)**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 3/4, 253–63, 9 figs. on 2 pls. [44 refs.]

CHAPMAN, J. S. & GUY, L. Ruth. **Scrofula caused by Atypical Mycobacteria.** *Pediatrics.* Springfield, Ill. 1959, Feb., v. 23, No. 2, 323–31, 3 figs. [13 refs.]

This paper gives a short clinical summary of this illness in 6 children, whose ages ranged from 20 months to 5 years. 3 of the children had discharging cervical lymphadenitis, 2 had abscesses in the mandibular area and 1 had a granuloma in the angle of the jaw; all were treated with isoniazid and PAS but X-ray therapy was given to 2 and from 1 the glands were removed. None of the children had evidence of pulmonary or bone disease and the Mantoux reaction varied from being negative to positive with 1 : 1,000 tuberculin. The onset of the disease was usually rapid and it was known to be associated with fever in 3 of the patients. There was no evidence of a similar infection or of tuberculosis in other members of the families.

The strains of mycobacteria isolated from the lesions produced an orange pigment; 5 were photochromogenic and the sixth was scotochromogenic. The colonies were moist and tended to confluence. [The rate of growth or whether growth occurred on nutrient agar is not stated.] Cording occurred but it was loose and thus distinctly different from the tight cording of H37Rv. The bacilli were catalase-positive and neutral red-positive, but the colour was brick-red rather than the true red of human and bovine tubercle bacilli. Morphologically, the bacilli were thicker, longer and more granular than H37Rv.

In the guineapig, 2 of the strains produced no lesions, 2 produced only a sinus at the site of inoculation, 1 produced lesions in the liver and the 6th strain produced lesions in the liver, glands, lungs and spleen; none of them produced widespread lesions in the rabbit when injected intravenously. Drug resistance was not an exceptional feature of these strains except that 2 were highly resistant to isoniazid, 1 being resistant to streptomycin.

Similar strains of mycobacteria were obtained from 3 swabs taken from the tonsillar crypts or pharynges of 43 healthy children, suggesting that the propharynx is the portal of entry of these organisms.

S. R. M. Bushby

LEBEK, G. Beitrag zur kulturellen Unterscheidung von säurefesten saprophytischen Mykobakterien und Tuberkelbakterien aus menschlichen Ausscheidungen. [**Cultural Differentiation of Acid-Fast Saprophytic Mycobacteria and Tubercle Bacilli from Human Specimens**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 3/4, 265–77. [87 refs.]

The English summary appended to the paper is as follows:—

"1. The possibilities of errors caused by saprophytes during the cultural isolation of tubercle bacteria, during the type differentiation of strains of tubercle bacilli, and during the determination of the sensitivity for tuberculostatic drugs are discussed, and examples are given.

"2. The following cultural tests are recommended for the differentiation of saprophytes and tubercle bacteria. The saprophytes will grow on Loewenstein-Jensen medium at 22°C. They are resistant to 100γ PAS on egg yolk media. They can multiply in sorbitolammonium chlorid solution at 37°C.*

"3. Saprophytic mycobateria grow quickly and produce pigments.

"4. Other tests for the differentiation of acid-proof mycobacteria and tubercle bacteria, e.g. the production of plaits in serum media, virulence tests and niacin test, can only be used with some caution. They contain possibilities for error."

"* With the exception of Mc fortuitum, which does not grow in sorbit nutritive solution."

TOLHURST, Jean C., BUCKLE, G. & WELLINGTON, N. A. M. **The Experimental Infection of Calves with** *Mycobacterium ulcerans*. *J. Hygiene.* 1959, Mar., v. 57, No. 1, 47–56. [11 refs.]

"Skin lesions with histopathology similar to that seen in lesions in man have been produced in calves by the experimental inoculation of cultures of *Myco. ulcerans*. Sensitization of infected calves to mammalian tuberculin as well as to ulceranin has been demonstrated.

"It is considered unlikely that cattle are a reservoir of infection for man."

VOGEL, H. **A Metabolic Study of Acid-Fast Bacteria from Cold-Blooded Animals.** *J. Infect. Dis.* 1959, Jan.–Feb., v. 104, No. 1, 28–37. [39 refs.]

CANNEFAX, G. R., ROSS, Hilary & BANCROFT, Huldah. **Reactivity of the RPCF Test in Leprosy compared with other Syphilis Tests.** *Pub. Health Rep.* Wash. 1959, Jan., v. 74, No. 1, 45–8. [11 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 728.]

BROWN, J. A. K. & STONE, M. M. **The Depot Lepromin Test and BCG Vaccination.** *Leprosy Review.* 1959, Apr., v. 30, No. 2, 110–11.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 729.]

GILLISSEN, G. & BIRKENHOVEN, E. Eine vergleichende Wertbestimmung von festen Spezialnährböden. [**A Comparative Assessment of Solid Selective Media**] *Arch. f. Hyg. u. Bakt.* 1958, June, v. 142, No. 4, 261–6, 1 fig. [21 refs.]

Parallel viable counts were done, on a range of different media, of suspensions of single strains of *Escherichia coli*, typhoid, paratyphoid A and paratyphoid B bacilli, *Salmonella enteritidis, Shigella sonnei* and *Sh. dysenteriae*. These organisms were first grown in broth, and towards the end of the log phase of growth appropriate dilutions prepared for dropping on to the various media. These included meat extract agar, a standard Merck agar, Endo medium, MacConkey agar, Kligler iron agar, Leifson medium, Drigalski-Conradi agar (a litmus lactose agar with crystal violet, which was omitted for the dysentery organisms) and Gassner agar (a metachrome yellow lactose agar with bromothymol blue as indicator).

The essential point about the results was the considerable inhibition caused by MacConkey and Leifson media as judged by the low viable counts obtained. Thus, with the strain of *Salm. typhi* used, the counts on these media were only one-quarter to one-third of the count on meat-extract agar. The author gives the results of mean counts on 10 replicate plates for each organism on each of the media tested, together with the standard deviations. His general conclusion is that one should bear in mind the relative advantages and disadvantages of the non-inhibitory and the more selective types of medium used in the isolation of pathogens from faeces. With the more selective medium a larger inoculum will to some extent compensate for the inhibition of the pathogenic organism. With less inhibitory media, spotting the pathogen colony will be more difficult but at least one will know that the organism in question is not likely to be inhibited by the component ingredients of the medium used.

B. Moore

OLITZKI, A. L. & OLITZKI, Z. **The Infection-Promoting Effect of Intermediates of the Tricarboxylic Acid Cycle on Pathogenic and Nonpathogenic** *Enterobacteriaceae*. *J. Infect. Dis.* 1959, Jan.–Feb., v. 104, No. 1, 5–12. [11 refs.]

"Some intermediates of the tricarboxylic acid cycle were utilized by all and others only by a part of enteric microorganisms as sources of energy. In vitro they inhibited the activity of guinea pig complement and the bactericidal action of normal rabbit serum. In this respect citric acid was the most active inhibitor due to its chelating activity. Its inhibitory effect was suspended in the presence of calcium chloride. Since citric acid also promoted infections of organisms

which in vitro were unable to utilize it, its infection-promoting effect may be ascribed partly to its anti-complementary and antibactericidal action."

MEISLOWA, Paula. Zagadnienie standaryzacji szczepionek durowych. I. Testy biologiczne na myszach. [**The Problem of Standardization of Typhoid Vaccines. I. Biological Tests in Mice**] *Med. Dośw. i. Mikrob.* Warsaw. 1958, v. 10, No. 3, 273–85. [33 refs.] English summary.

A comparison has been made of active and passive immunization tests in mice in the evaluation of the antigenicity of endotoxic typhoid vaccine, both alone and combined with tetanus toxoid and alcohol-treated typhoid vaccine. In the active immunization tests the total mortalities in 234 mice immunized with 3 dose levels of all the vaccines used in the investigation and challenged 2 weeks later with a virulent strain of *Salmonella typhi* ranged from 6·7 to 29·6%, compared with 86·1% in a control group of 108 unimmunized mice. The test enabled the antigenicity of the vaccines to be satisfactorily evaluated. The results obtained in passive immunization tests are also presented. *D. J. Bauer*

GUPTA, S. P., GUPTA, N. P. & MULLICK, K. S. **Preparation of an Adsorbed Vaccine for Typhoid, Cholera and Dysentery.** *J. Indian Med. Ass.* 1958, June 1, v. 30, No. 11, 343–7.

Extracts of *Salmonella typhi, Salm. paratyphi A, Shigella dysenteriae* and *Vibrio cholerae* were prepared by extraction with water, sodium acetate, diethylene glycol, trichloracetic acid and by tryptic digestion. They were adsorbed onto a calcium phosphate precipitate and tested for antigenicity by subcutaneous injection of rabbits.

The trichloracetic acid extracts of *Salm. typhi* gave a good O-agglutinin response and the antibody protected mice in passive-protection tests. The tryptic digest extracts were less effective and the other extracts had little or no antigenicity.

Only a poor antibody response was obtained with the extracts of *Salm. paratyphi A, Sh. dysenteriae* and *V. cholerae.* *J. Nagington*

RAUSS, K., KÉTYI, I. & RÉTHY, L. Untersuchungen über die Entgiftung und Adjuvierung von enteralen Impfstoffen. [**The Effect of Adjuvants and Detoxification on Enteric Vaccines**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, Sept., v. 116, No. 3, 276–86, 1 fig. [21 refs.]

The authors investigated the toxicity and immunogenicity of a mass vaccine against dysentery, typhoid and tetanus prepared with an aluminium hydroxide gel of a type already used in Hungary in combined prophylactics against diphtheria, pertussis and tetanus. The antigen was to include *Shigella sonnei, Sh. flexneri* types 2a and 3, *Salmonella typhi* and tetanus toxoid.

Boivin antigens of the 4 organisms were prepared, and tetanus toxoid prepared by standard procedures. Adsorbates were made with different concentrations of aluminium hydroxide. Toxicity was measured by intraperitoneal mouse inoculation, and antigenicity by challenging subcutaneously immunized mice with 250–500 LD50, suspended in mucin, a week after the immunizing injection.

The authors tabulate first the results obtained with the *Sh. flexneri* type 2a antigen. A 5 mgm. dose of aluminium hydroxide per ml. of Boivin antigen gave maximal adsorption. Detoxification increased in proportion to the amount of aluminium hydroxide added: 3·75–5 mgm. reduced toxicity 8-fold, 10 mgm. 9-fold and 20 mgm. 10-fold. Alum precipitation, on the other hand, only halved toxicity. Immunogenic potency in mice reached a clear-cut peak at the 3·75–5 mgm. level, when potency was 12 times that of unadsorbed antigen and 2·5 times that of alum-precipitated antigen. If more than 5 mgm. of aluminium hydroxide per ml. of Boivin antigen were used, antigenicity fell away steeply.

Similar results were obtained with the other shigellae; with typhoid antigen detoxification was less successful.

A mixed antigen containing Boivin extracts of the 4 bacterial species and tetanus toxoid gave results very similar to those obtained with the individual antigens. Toxicity of the mixed vaccine was reduced 6-fold and antigenicity increased 5 to 25-fold for the different antigens as compared with unadsorbed antigens. The antigenicity of this product was about 3 times that of alum-precipitated prophylactic. *B. Moore*

RAUSS, K., KÉTYI, I., RÉTHY, L. & JOÓ, I. Über die Herstellung, Impfreaktionen und Immunisierungsfähigkeit des kombinierten Typhus-Dysenterie-Tetanus-Impfstoffs. [**The Preparation, Side-Effects and Antigenicity of Combined Typhoid-Dysentery-Tetanus Vaccines**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, Sept., v. 116, No. 3, 287–307. [25 refs.]

The authors do not accept the thesis that humoral antibodies play no part in protection against dysentery. Rauss and Kétyi [this *Bulletin*, 1956, v. 31, 121] found that the blood of dysentery patients contained type-specific mouse protective antibodies which increased in titre into convalescence and took 10–12 months to fall to pre-infection levels. They think therefore that dysentery prophylaxis is a matter of finding a more effective antigen.

Various age-groups were inoculated with vaccines prepared as in the above paper. 3 test prophylactics were used: P 15, which contained the concentration of aluminium hydroxide gel giving optimal antigenicity and reducing toxicity 6-fold; P 20, which contained double the antigen and gel concentrations of P 15; and P 14, which contained the same amount of antigen as P 15 but twice the gel concentration. Preliminary study of P 14, P 15 and P 20 showed 8-, 6- and 6-fold levels of detoxification and 6-, 10- and 5-fold increases respectively in immunogenicity.

Adults, children aged 12–13 and younger children of 1–3 years were given 2 inoculations of combined typhoid-dysentery-tetanus vaccine with a 4-week interval. As control prophylactics the authors used an

alum-precipitated typhoid-tetanus vaccine and an alum-precipitated typhoid vaccine, and in adults a combined typhoid-paratyphoid-dysentery-cholera-tetanus vaccine. About 10,000 subjects were vaccinated in all, and observations were made on groups averaging 100 persons each.

Of 99 adults inoculated with P 14, only 6 showed local reactions after 24 hours, and the corresponding figures for P 15 and P 20 respectively were 2/97 and 8/98. In marked contrast, 103 out of 145 adults showed a local reaction after the control combined vaccine, and 90 a general reaction. In the 12–13 age-group, the incidence of local and general reactions and of absence from school were as follow:—

Antigen	Total No. of children	Local reaction	General reaction	Absent from school
P 14	120	3	2	16
P 15	124	19	13	13
P 20	129	13	17	16
Alum-ppt. typhoid-tetanus	118	26	2	40
Alum-ppt. typhoid	118	26	28	54

In the 1–3 age-group, only 4 out of 86 inoculated with P 15 showed a local reaction.

Serum pools were made of groups of about 100 vaccinated subjects, with blood collected before inoculation and 2 weeks after the second dose. These pools were tested for mouse-protective antibody. The protective potency of the typhoid and tetanus components in children was compared to that evoked by ordinary commercial alum-precipitated vaccines and in the adults by the effects of vaccination with the mixed vaccine described above. To estimate the effectiveness of dysentery prophylaxis, the protective power of the sera of vaccinated subjects was compared to that of the sera of dysentery convalescent patients.

In adult subjects, inoculation with P 15 increased the protective antibody titres against the various shigella components 17–56-fold. This was statistically highly significant. P 14 and P 20 were less effective, and the titre differences before and after inoculation were not significant, although greater than after inoculations with the control vaccines. The titres of vaccinated subjects in shigella antibody were very similar to those found in dysentery convalescents. Typhoid antibody titres also rose satisfactorily in the various age-groups. In children aged 1–3 years, shigella antibodies showed a significant increase in children without a recent history of dysentery but not in those who had recently suffered from dysentery. *B. Moore*

MEGAY, K., MAREK, A. & GRIMS, T. T.P.E.-Diagnostik aus angetrockneten Stuhlproben. [**The Isolation of *Salmonella* Strains from Dried Stool Specimens**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 3/4, 218–28, 8 figs.

The English summary appended to the paper is as follows:—

"Investigations were undertaken concerning the problem whether Salmonella strains could be isolated as frequently from stool specimens dried on cardboard as from specimens collected in usual containers. Stools were infected artificially. The specimens were stored at different temperatures for six days. The number of positive results was at least the same with both groups stored at low temperatures. The dried specimens gave more positive results when stored at higher temperatures. Stool containers made of water-proof cardboard were described."

STAUB, A. M., TINELLI, R., LÜDERITZ, O. & WESTPHAL, O., with the technical collaboration of B. LELUC. Étude immunochimique sur les *Salmonella*. V. Rôle de quelques sucres, et en particulier des 3–6 didésoxyhexoses, dans la spécificité des antigènes O du tableau de Kauffmann-White. [**Immunochemical Studies on *Salmonella*. V. Role of Certain Sugars, particularly 3–6 Didesoxyhexoses, in the specificity of Kauffmann-White O Antigens**] *Ann. Inst. Pasteur.* 1959, Mar., v. 96, No. 3, 303–32, 2 figs. [43 refs.]

These workers have previously demonstrated the presence in salmonella organisms of 4 new sugars (didesoxyhexoses): tyvelose, abequose, paratose and colitose. In collaboration with C. FOUQUEY, E. LEDERER *et al.* (*C.R. Acad. Sci.*, 1958, v. 246, 2417; *Nature*, 1958, v. 182, 944) the exact nature of these sugars was determined and their synthesis effected. In this communication Mme. Staub and her colleagues report the results of their studies of these sugars and of glucose and rhamnose in precipitation inhibition procedures which can be related to specific O-antigen fractions of salmonella organisms, as set out in the Kauffmann-White scheme.

For instance they show that the precipitation of an anti-typhoid O serum (horse) by a specific typhoid polysaccharide extract was largely inhibited by the didesoxyhexose, tyvelose (whether this was the natural sugar separated chromatographically from the *Salmonella typhi* polysaccharide or the synthetically prepared sugar), whereas the other didesoxyhexoses, and glucose or rhamnose had little effect. This inhibition was particularly marked with extracts oxidized by periodic acid, where O-factor 9 was predominant, so that it appeared that tyvelose was specifically associated with O-factor 9. Similarly it was shown that the abequose played the same role with regard to the B-group O-antigen 4. The role of paratose in relation to O-factor 2 (*Salm. paratyphi A*) could not be so clearly defined. It would seem that the antigen complex 12 ($12_1,12_2,12_3$) is associated with the presence in the polysaccharide extracts of *Salm. typhi* (9,12) and *Salm. paratyphi B* (4,12) of 2 side-chains—one terminating in rhamnose and the other in glucose.

2 other points of considerable interest emerge from these studies. In 1926 Bruce WHITE [this *Bulletin*, 1927, v. 2, 96] noted the antigenic relationship between *Salm. paratyphi B* and Salm. Newport, an irregular relationship, which, however, with some strains may be very marked. It is satisfactory that the authors were able to relate this cross-reaction to the presence of

abequose in polysaccharide extracts of salmonella organisms belonging to the O-sub-group C_2. The second point is concerned with the identical O-antigens carried by Salm. Adelaide and *Escherichia coli* O 111 and the demonstration that the cross reactions between the two organisms is related to the presence of colitose in the polysaccharide extracts of both strains.

The Kauffmann-White classification of the salmonella organisms was founded solely on serological reactions and is sometimes criticized because of this. Mme. Staub and her colleagues bring forward evidence from their immunochemical studies that would appear to place the classification of the somatic antigens on a firmer basis. *H. J. Bensted*

Brandis, H. Die Typendifferenzierung von Typhus- und Paratyphus-B-Stämmen mit Bakteriophagen (Lysotypie). [**Bacteriophage Typing of** *Salm. typhi* **and** *Salm. paratyphi B* **Strains**] *Deut. med. Woch.* 1958, Oct. 31, v. 83, No. 44, 1925–8, 1962. [12 refs.]

This is a useful account, written for general practitioners, of the phage typing of enteric strains. As an example of the epidemiological value of this technique, the author cites recent German work linking paratyphoid fever with the use of Chinese egg. [Brandis, this *Bulletin*, 1958, v. 33, 784; Schmidt & Lenk, *Zent. f. Bakt.*, 1957, v. 170, 543.]

The different phage types of *Salm. typhi* and *Salm. paratyphi B* are listed, and a general commentary is given on the prevalence of the various types in Germany in recent years. Little change has occurred since 1950 in the proportions of the different phage types of typhoid bacillus isolated. The usefulness of subtyping type E_1 and of the subtyping of type A strains by Nicolle's methods are mentioned. A similar discussion of the epidemiology of paratyphoid B infections follows.

During 1955–6, the author typed 17 typhoid and 609 paratyphoid B strains isolated from river and other surface waters. Every epidemiologically significant phage type of paratyphoid bacillus other than type 2, the type associated with Chinese egg, was found in this series of strains. *B. Moore*

Gherman, D., Zalman, M., Levin, S. & Petrilă, I. Contribuţii la studiul metodelor de depistare a excretorilor de bacili tifici în mediul rural. [**Contributions to the Study of Methods of detecting Typhoid Carriers in Rural Areas**] *Microbiol., Parazitol si Epidemiol.* Bucharest. 1958, May–June, v. 3, No. 3, 247–55. [12 refs.]

In 1953–4 an epidemiological investigation was carried out in an endemic focus of typhoid in Rumania. In serological examinations carried out on 130 persons agglutinin to the Bhatnagar Vi strain of *Salmonella typhi* was found in 11 of 19 (58%) persons who had previously had typhoid, in 26 of 46 (56%) contacts and in 24 of 65 (37%) industrial workers. A somewhat lower percentage of positive results was obtained in tests with *Salm. ballerup.* Stool cultures were carried out in 183 instances, and 12 strains of *Salm. typhi* were isolated from 11 persons who were evidently carriers, including 6 persons who had had the disease, and 5 contacts; 2 strains were of type E_1 and 6 were type A. On isolation 8 strains did not possess Vi antigen and 10 did not possess H antigen, although H antigen could be recovered on passage in 7 instances; 4 strains were isolated from persons in whom Vi agglutinin could not be demonstrated. *D. J. Bauer*

Orlova, T. G. **Virulence and Antigenicity of** *Salmonella typhosa* **Strains and Antigenicity of the Corresponding Vaccines in relation to Content of VI Antigen as estimated by means of the Haemagglutination Reaction.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1288–93. [Translated from Russian.]

Vi-antigen extracts were prepared from different strains of *Salmonella typhi* by making saline suspensions of freshly grown cultures with bacterial cell concentrations of 10^9, allowing them to stand at room temperature for 1 hour, centrifuging to throw down all the bacterial cells and using the supernatants from the various cultures as the antigens to be assayed by the haemagglutination test, which employed sensitized fowl red blood cells and rabbit Vi immune serum. The titre of each Vi-antigen extract was taken from the dilution of the extract which gave a corresponding haemagglutination reaction with the same dilution of the antiserum in the chess-board test. Thus if 1/80 antigen gave a +++ reading with 1/80 serum and a 1/160 antigen gave only + agglutination with a 1/160 serum the titre of the antigen was taken to be 1/80. With the antigen titre as a yardstick the virulence and antigenicity of different cultures were compared and the antigenicity of vaccines expressed in terms related to the amount of Vi-antigen in the vaccines and their mouse protection activity.

The results were in general agreement with those of other workers and the author concludes that vaccines with a low Vi-antigen content have a low protective value, but it did not always follow that the vaccine with the highest Vi-antigen content was the most efficient when tested against the reference vaccine. [Incomplete references appear in the text, but the usual list of complete references is not set out at the end of this English version.] *H. J. Bensted*

i. Public Health Lab. Service. *Salmonella* **Organisms in Animal Feeding Stuffs and Fertilizers.** Report of a Working Party [Walker, J. H. C., Chairman]. *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Feb., v. 18, 26–35.

ii. Newell, K. W., McClarin, R., Murdock, C. R., MacDonald, W. N. and Hutchinson, H. L. **Salmonellosis in Northern Ireland with special reference to Pigs and** *Salmonella*-**Contaminated Pig Meal.** *J. Hygiene.* 1959, Mar., v. 57, No. 1, 92–105. [27 refs.]

i. The Public Health Lab. Service working party undertook the examination of a wide variety of animal feeding stuffs and fertilizers used in Britain for the

presence of salmonella organisms because individual reports had indicated a very high salmonella-contamination rate in constituents of some of these products, and it seemed desirable to obtain a more comprehensive picture. The examinations covered hoof and horn, blood, bone, meat, fish, vegetable and milk products, whether used for feeding stuffs or fertilizers, and certain organic compounds produced by the fertilizer industry. Although most of the bone and meat products used in this country are home-produced, some bone meal and the greater part of the fish meal is imported. It is therefore difficult to determine with certainty the source of every constituent of some proprietary food stuffs.

Apart from milk products, which were free from salmonellae, contamination was widespread and out of some 1,200 specimens of all types salmonella organisms were isolated from 24%. Bone products and fish meal, irrespective of source, were all contaminated, but the imported products more heavily: fish meal from Angola 73%, bones or bone meal from India 100% and bones or bone meal from Argentina 81%. The wide variety of salmonellae that may be found in bone or fish meal is illustrated by the fact that the 194 salmonella isolations from 651 specimens of these products comprised 72 different sero-types.

ii. The report of this working party was not concerned with relating their findings to epidemiological problems, but Newell and his colleagues in their paper attempt to relate salmonella-contaminated feeding stuffs to the salmonella infection of pigs and, in turn, to outbreaks of salmonellosis in the human population, although their investigations began in the slaughter-house and then proceeded to incriminated farms. Here healthy pigs and the various pig meals were examined bacteriologically and to a large extent they were successful in isolating the same salmonella serotypes from the pigs that were found in the pig meals. It was not possible in any case to demonstrate a complete chain from contaminated pig-meal→infected pig→contaminated meat in slaughter-house→food-poisoning in man with a common salmonella sero-type throughout; there was always one link missing, but the evidence was very strong. There seems to be little doubt, for instance, that cases of food-poisoning due to *Salmonella orion* could be related to pig meat infected with this organism, but the time-lag and the great variation in the salmonella flora of Angolan fish meal (the incriminated foodstuff) from different, and even the same, batches resulted in the broken link in the chain of evidence.

The paper by Dr. Newell and his colleagues provides a valuable addendum to the Public Health Lab. Service working party's survey of the salmonella contamination of animal feeding stuffs and indicates that the latter's findings must be considered to have epidemiological significance. *H. J. Bensted*

STOKES, J. L. & BAYNE, H. G. **Dwarf Colony Mutants of Salmonellae.** *J. Bacteriology.* 1958, Aug., v. 76, No. 2, 136–41, 3 figs. [18 refs.]

Dwarf colony variants of 10 salmonella serotypes were produced by incubation of cultures at 35°C. in nutrient broth containing 1% of either lithium sulphate or sodium selenite. Usually dwarf colonies appeared after 1–2 weeks when the lithium sulphate cultures were plated onto trypticase soy agar. They occurred less often from the selenite and never from nutrient broth which contained neither substance.

Serologically and morphologically the mutants resembled their parents but they fermented carbohydrates and oxidized amino acids much more slowly. The mutants of Salmonella Anatum and Salm. Oranienburg required cystine for growth, that of Salm. Meleagridis required cystine and pyridoxine and that of Salm. Barielly required cystine and several other amino acids.

This suggests that the small colonies are the result of slower growth due to the inadequate amount of these growth factors in conventional media.

J. Nagington

RIBI, E., MILNER, K. C. & PERRINE, T. D. **Endotoxic and Antigenic Fractions from the Cell Wall of *Salmonella enteritidis*. Methods for Separation and some Biologic Activities.** *J. Immunology.* 1959, Jan., v. 82, No. 1, 75–84, 3 figs. [29 refs.]

Deflagellated *Salmonella enteritidis* were obtained from freshly grown cultures suspended in saline or distilled water by repeated centrifugation and washing. The washed bacterial cells were then disrupted in a Mickle tissue disintegrator with glass beads and afterwards subjected to differential centrifugation by which means relatively pure preparations of cell wall and cell protoplasm were obtained. The effectiveness of the procedures was checked by electron microscopy.

When suspensions in water of live cells or suspensions of cell walls not fixed in formalin were saturated with ethyl ether, soluble endotoxin was released into the aqueous phase. O-antigen of low toxicity could be extracted from the intact cell or the cell wall by means of aqueous dioxane.

The biological analysis of the various fractions obtained showed that the cell protoplasm was relatively free from toxicity, showed little or no reaction with specific O-antibody and was very poor as an immunizing agent. Preparations of cell walls, on the other hand, were more toxic than preparations of whole cells, showed about the same degree of reaction with O-antibody, but were far more efficient as immunizing agents. The dialysed aqueous ether extract was highly toxic for mice but less efficient as a protective vaccine; the endotoxin obtained by this method is considered to equal the Boivin extract and to be easier to prepare. Adequate evidence is produced to indicate that the toxic and immunogenic properties of living cells of deflagellated *Salm. enteritidis* are restricted to the bacterial cell wall. It should be noted that the physico-chemical state of endotoxin or O-antigen in living cells must differ from that in killed cells. *H. J. Bensted*

GROSZ, H. J. & NORTON, J. **Effect of Chlorpromazine on *Salmonella enteritidis* Infection in Mice.** *Science.* 1959, Mar. 20, v. 129, 784–5.

"Chlorpromazine increases the susceptibility of mice to infection with *Salmonella enteritidis*."

LIBERMAN, Rose, EARLE, H., IKARI, N. & MCCULLOUGH, N. B. **Immunity afforded by specifically absorbed, unabsorbed and Combinations of *Salmonella* Antisera.** *J. Immunology.* 1959, Jan., v. 82, No. 1, 52–61, 3 figs. [20 refs.]

The passive mouse protection test was employed to study the relationships of the major antibody components of *Salmonella enteritidis* and *Salm. typhi-murium* in rabbit immune sera in protection experiments with mucin-treated suspensions of living organisms as the challenge. The antisera represented pure O-Factors 4 or 9; 4·12; 9·12 and various combinations so that the components 12_1,12_2 were increased in mixtures of 2 immune sera. The results showed that the single Factor 9 serum gave a significantly greater degree of protection against challenge with the homologous organism than the native *Salm. enteritidis* serum whereas single Factor 4 serum gave less protection than the whole unaltered *Salm. typhi-murium* serum against the homologous challenge. Increasing the amount of 12_1,12_2 antibody by mixing native *Salm. typhi-murium* and *Salm. enteritidis* sera in different proportions showed enhanced protection but this enhancement did not appear to be due solely to the amount of these two components in the serum mixtures and was independent of complement. No satisfactory explanation is offered for the very significant difference in the protective value of the two absorbed sera—single Factor 4 and single Factor 9—although it is suggested that the absorption of *Salm. enteritidis* serum for the production of the single Factor 9 serum could have removed an interfering agent present in the untreated serum against that organism but which was not present in the untreated *Salm. typhi-murium* serum.

H. J. Bensted

GÄRTNER, H. & BÖHLCK, I. Epidemiologische Beobachtungen über das Auftreten von Salmonella Java und Untersuchungen an 23 Stämmen. [**Epidemiological Observations on Salm. Java Infections and a Study of 23 Strains**] *Arch. f. Hyg. u. Bakt.* 1958, Sept., v. 142, No. 6, 415–19. [12 refs.]

The authors report on 23 strains of Salmonella Java of which 20 were isolated from persons concerned in a small outbreak in the Saar. Probably many more people were involved but the episode came to notice rather late as, apart from one schoolgirl with a paratyphoid-like illness lasting 10 days, the other cases investigated had only mild or subclinical attacks. 2 further strains of the organism were isolated from sewage works effluents, and the last one from the stools of a carrier who had probably been infected in eastern Europe and excreted the organism for at least 2 years.

All 23 strains produced no slime wall and showed a characteristic colonial morphology, growing as radially striated colonies which became membranous after a few days' incubation and lifted off the culture medium when touched with a loop. All were d-tartrate positive. Inosite was fermented by the epidemic strain but not by the other 3. and rhamnose by all except the carrier strain. Serologically, all strains had the antigenic structure 4,5,12 : b : 1,2. The epidemic strain fell into *Salm. paratyphi B* phage type 1 var. 3 and the carrier strain into type $3a_1$, var. 1.

B. Moore

MICHAEL, J. G. & BRAUN, W. **Serum Spheroplasts of *Shigella dysenteriae*.** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 422–5, 2 figs.

Type-strains of Shiga's dysentery bacillus were grown on tryptose-agar at 37°C. for 18–24 hours and exposed to the bactericidal action of normal human serum in either tryptose-broth or a suitable buffer solution with the addition of various concentrations of carbohydrates. After different periods of exposure the various bacterial suspensions were plated out and the resulting growths were examined under the phase-contrast microscope.

It was found that while 20% sucrose protected the organism against the bactericidal action of the serum and permitted survival, the other carbohydrates—lactose, starch, galactose or glucose—in concentrations from 10 to 20%, afforded no such protection. Microscopical examination showed that this sucrose protection involved the prevention of lysis of the wall-deficient bacterial cells. The production of spheroplasts, under the influence of normal serum with 20% sucrose, differed from penicillin protoplasts or spheroplasts in that the exponential phase of growth was most suitable for the latter whereas the stationary stage of growth was best for the production of serum spheroplasts.

Sucrose could protect against the bactericidal effect of either serum alone or penicillin alone but failed against the combined effect of serum plus penicillin.

H. J. Bensted

GILLIES, R. R. & DUGUID, J. P. **The Fimbrial Antigens of *Shigella flexneri*.** *J. Hygiene.* 1958, Sept., v. 56, No. 3, 303–18, 6 figs. on 3 pls. [18 refs.]

The fimbriae of *Shigella flexneri* types 1a, 2b, 3, 4a and 5, irrespective of the O-serotype, are antigenically identical. They contain one major *flexneri* antigen which was detected in only one strain of *Escherichia coli* [see DUGUID *et al.*, this *Bulletin*, 1956, v. 31, 861], one or more minor *flexneri-coli* antigens shared with most *E. coli* strains and at least one other antigen shared with a few *E. coli* strains.

Agglutination of fimbriate *Sh. flexneri* by homologous antiserum is mainly due to the fimbriae. It occurs more rapidly than O-agglutination and to a higher titre. It is loosely floccular and is not specific. It obscures O-agglutination but never enough to produce complete O-inagglutinability.

To avoid fimbriate agglutination non-fimbriate suspensions should be used, prepared by selection of colonies from dry agar plate cultures or by boiling the suspension followed by centrifugation to remove the detached fimbriae.

Fimbrial antigens do not appear to correspond to any of the K antigens which have been described, *i.e.* L, A and B but they closely resemble the X-antigen first described in salmonellae by TOPLEY and AYRTON (*J. Hygiene*, 1924, v. 23, 198).

80 of 81 normal human sera, mainly antenatal specimens, contained fimbrial agglutinins to *Sh. flexneri* at titres from 1 in 30 to 1 in 1,920, usually around 1 in 240.

J. Nagington

SIMMONS, D. A. R. **The Serological Specificity and Cross-Reactivity of some *Shigella flexneri* Extracts.** *Brit. J. Exper. Path.* 1958, Oct., v. 39, No. 5, 497–501, 1 fig. [10 refs.]

Trichloracetic acid extracts of the somatic antigens and their polysaccharide components were made of *Shigella flexneri* types 1a, 2a, 3, 4a, 5, 6 and the X and Y type variants.

The serological reactions of these extracts were compared with the reactions of alcoholized whole bacteria and it was found that they behaved in a very similar manner.

This confirms the findings of other workers in which only a few of the *Sh. flexneri* serotypes were examined and extracts were made with other solvents such as hydrochloric acid, pyridine and diethylene glycol [this *Bulletin*, 1946, v. 21, 540; 1947, v. 22, 151 *bis*.]

J. Nagington

OKABE, K. **Antigenic Variation in relation to Classification of *Shigella flexneri*.** *J. Immunology.* 1958, Oct., v. 81, No. 4, 285–91. [16 refs.]

Variant strains of *Shigella flexneri* were produced by serial subcultures in broth to which single factor rabbit antiserum had been added. The best results were obtained with 1% or more of antiserum in a tryptose-phosphate broth and subculture every 8 hours after shaking and then allowing the broth to stand for 1 hour to settle.

To explain the antigenic variants produced the author considers that there are 3 phase variations in *Sh. flexneri* instead of the generally accepted 2 and that the antigenic components can be classified into 3 groups—primary, secondary and tertiary.

In phase A the primary antigens are dominant and lost in the phase change A–B. In phase B the secondary antigen, which was previously potentially present, becomes dominant; and in the same way the tertiary antigen becomes dominant following the loss of the secondary in the B–C change.

The primary antigens include the usual 6 type-specific antigens, the group antigen 6 and factor X, the secondary antigen is Y and the tertiary antigen is a new one designated C.

J. Nagington

MCGUIRE, C. D. & FLOYD, T. M. **Studies on Experimental Shigellosis. I. *Shigella* Infections of Normal Mice.** *J. Exper. Med.* 1958, Aug. 1, v. 108, No. 2, 269–76. [10 refs.] **II. The Effect of Fasting and Fatigue on *Shigella flexneri* 3 Infections in Mice.** *Ibid.*, 277–82.

Experimental infection of normal mice with *Shigella flexneri* type 3 was demonstrated. The LD50 at 24 hours for oral challenge was $4{\cdot}8 \times 10^9$, for rectal inoculation of the transverse colon $2{\cdot}8 \times 10^8$ and for intraperitoneal challenge $4{\cdot}4 \times 10^8$ viable organisms.

It was not possible to kill mice with heat-killed suspensions given orally but by the other routes a dose of about 10 times the viable dose was fatal.

All the animals injected intraperitoneally with viable organisms had a bacteraemia for 6 hours or longer. Nearly all of those inoculated rectally also had a bacteraemia and in 75% of them it persisted for 24 hours. Oral challenge was less likely to cause a bacteraemia.

About half of the orally infected animals had enlargement of the spleen and liver before death and in about one-third of them there was some diarrhoea.

The parenteral LD50 was reduced to about half when the mice were starved for 24 hours and it was further halved when they were starved for 48 hours.

The oral LD50 was doubled by starvation, presumably because of an increased bactericidal action of the gastric contents. There was an increased incidence of bacteraemia in such mice and there was a greater and more prolonged intestinal infection. Fatigue had a less pronounced effect than starvation on susceptibility.

J. Nagington

SERÉNY, B. **Acquired Natural Immunity following Recovery from Keratoconjunctivitis Shigellosa.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 4, 343–58. [19 refs.]

The author found that experimental infection of guineapigs by direct instillation of suspensions of living cultures of *Shigella flexneri* 3, into one of the eyes, resulted in significant local immunity which appeared to be non-specific in nature; the immunity with regard to the opposite eye was less marked but seemed to be specific and the presence in the blood serum of agglutinins and mouse-protecting antibodies, which were specific in nature, would confirm this. Clinical immunity resulting from the original experimental infection, although locally significant in a non-specific form, was of a relatively low grade when examined for general specific immunity.

The author suggests that this type of experimental work could be used for the study of immunity of bacillary dysentery in man. While this may be true it seems doubtful if the comparatively rare post-dysenteric conjunctivitis is imitated exactly by instilling bacterial cultures into the eyes of guineapigs.

[See also this *Bulletin*, 1958, v. 33, 690.]

H. J. Bensted

GOLBA, J., CHOJNACKA, Lucyna & KLECHA, I. Epidemia wonda czerwonki bakteryjnej w zakładzie przemysłowym. **[A Water-Borne Epidemic of Bacillary Dysentery in a Factory]** *Przegląd Epidemiol.* Warsaw. 1958, v. 12, No. 2, 115–22, 1 fig. English summary (7 lines).

In May 1956 an outbreak of bacillary dysentery occurred among the workers in a factory in Szczecin, Poland. The first cases appeared after damage to a deep well supplying the factory when unchlorinated canal water taken from near its own sewer outfall was brought into use for manufacturing processes, and was used by the employees for washing and drinking in

spite of instructions to the contrary. 486 cases occurred in all. After the peak of the epidemic the clinical aspects of the disease changed, and *Salmonella typhi-murium* could then be isolated from the stools. In an examination of the stools of 255 patients *Shigella flexneri* was isolated in 27 instances, *Sh. schmitzii* [*Sh. dysenteriae* 2] in 1, *Salm. paratyphi B* in 2 and *Salm. typhi-murium* in 12 instances. 2 strains of *Sh. flexneri* were isolated from 10 samples of canal water.

D. J. Bauer

GRAHAM, J. M. **An Outbreak of Dysentery due to a Non-Mannitol-Fermenting Strain of** *Shigella sonnei*. *J. Path. & Bact.* 1958, July, v. 76, No. 1, 291–3.

HUGO, W. B. & LUND, Barbara M. **The Effect of Supplementation of the Growth Medium with Yeast Extract, on Dehydrogenase Activity of** *Escherichia coli*. *J. Applied Bact.* 1958, Dec., v. 21, No. 2, 249–56, 4 figs. [16 refs.]

NEIDLE, A. & WAELSCH, H. **The Origin of the Imidazole Ring of Histidine in** *Escherichia coli*. *J. Biol. Chem.* 1959, Mar., v. 234, No. 3, 586–91. [40 refs.]

LITTAUER, U. Z. & EISENBERG, H. **Ribonucleic Acid from** *Escherichia coli*. **Preparation, Characterization and Physical Properties.** *Biochim. et Biophys. Acta.* 1959, Apr., v. 32, No. 2, 320–37, 9 figs. [56 refs.]

SCHWARTZ, J. H., MAAS, W. K. & SIMON, E. J. **An Impaired Concentrating Mechanism for Amino Acids in Mutants of** *Escherichia coli* **resistant to L-Canavanine and D-Serine.** *Biochim. et Biophys. Acta.* 1959, Apr., v. 32, No. 2, 582–3.

HEDEGAARD, J., BEAU-THOMÉ, Françoise, THOAI, Nguyen-van & ROCHE, J. Influence de l'histidine et ses métabolites sur la biosynthèse des purines par *Escherichia coli* B. II. Influence de l'histidine sur la formation de la 5(4)-amino-4(5)-imidazolecarboxamide en présence de la sulfadiazine. *C.R. Soc. Biol.* 1958, v. 152, No. 12, 1673–7, 1 fig. [32 refs.] III. Mode d'action de l'histidine dans la biosynthèse de la 5(4)-amino-4(5)-imidazolecarboxamide. *Ibid.*, 1712–16, 1 fig. [19 refs.] [**Influence of Histidine and its Metabolites on the Biosynthesis of Parines by** *Escherichia coli* **B. II. Influence of Histidine on the Formation of 5(4)-amino-4(5)-imidazolecarboxamide in the Presence of Sulphadiazine. III. Mode of Action of Histidine in the Biosynthesis of 5(4)-amino-4(5)-imidazolecarboxamide.**]

SNELL, J. F. & CHENG, Lorraine. **Studies in Metabolic Spectra. III. The Accumulation of D-Glutamic Acid in Oxytetracycline-Treated** *Escherichia coli*. *Antibiotics & Chemotherapy*. New York. 1959, Mar., v. 9, No. 3, 156–9.

GUHA, G. **Temperature Tolerance and Kinetics of Thermal Inactivation in** *E. coli communior* **Phage of Various Concentrations.** *Proc Soc. Exper. Biol. & Med.* 1959, Mar., v. 100, No. 3, 487–9, 3 figs.

HÖSEL, G. Experimentelle Studien zur Abgrenzung des Begriffes des sogenannten Coliwertigkeit. I. Mitteilung. Zielsetzung, Untersuchungsmaterial und Versuch einer Abgrenzung mit den üblichen Untersuchungsverfahren. [**Experimental Studies on the so-called evaluation of** *Escherichia coli* **Strains. I. Attempts at Differentiation by the use of Ordinary Diagnostic Methods**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 7/8, 480–7. II. Mitteilung. Typenbestimmung auf Endoagar und *coli* Index. [**Type Differentation on Endo Agar and by the** *coli* **Index**] *Ibid.*, 487–94. III. Mitteilung. Studien über den Wirkungsmechanismus bei der *coli* Index bestimmung. [**Factors affecting the Determination of the** *coli* **Index**] *Ibid.*, 494–504. IV. Mitteilung. Colizinbildung und Colizinempfindlichkeit der Colistämme. [**Production of and Sensitivity to Colicines in the** *coli* **Strains**] *Ibid.*, 505–16, 8 figs.

For more than 40 years, German workers have fed living suspensions of *Escherichia coli* strains to dyspeptic patients. Methods purporting to differentiate between strains appropriate to this purpose and unsuitable ones have been described, but the more modern techniques for the classification of coliform organisms have never been critically applied by the devotees of this form of therapy. In the present work the author examined 100 strains of *E. coli* by various methods. The series comprised 29 strains from a collection of stock cultures including 5 of pathogenic *coli* and 4 strains considered suitable for oral administration by prominent workers in this field; 47 strains isolated from stools submitted for routine examination, 10 from the stools of healthy subjects and various other strains isolated from sewage and from the faeces of hamsters, mice and birds. All these strains were MR positive, VP negative, indole positive, H_2S negative, urease negative and citrate negative. They were in addition tested in a wide range of sugars, for motility and for haemolytic activity against horse red cells. None of the various tests differentiated between pathogenic *coli* strains and those reputed to be suitable for oral administration to dyspeptic subjects.

The methods used in selecting strains of *E. coli* for oral therapy include the study of colonial morphology on Endo's medium and determination of the "*coli* index", a measure of the capacity of a given strain to outgrow typhoid bacilli in mixed culture in peptone water. The author failed to establish any colonial differences on Endo's medium. The *coli* index was equally unsatisfactory, as successive determinations of this index with a given pair of strains yielded discrepant results. Moreover, by the usual interpretation of the *coli* index figure, some pathogenic *coli* strains would have been considered more suitable for oral therapy than strains of *E. coli* that had been used for this purpose for many years.

More detailed study of the *coli* index technique, discussed in the author's third paper, showed that the relative numbers of *coli* and typhoid bacilli present in mixed culture varied during the period of incubation, so that the *coli* index figure obtained depended on the precise time of subculture. The author also found that when broth cultures of typhoid bacilli were added to *coli* cultures and the mixed suspension immediately plated out, recovery of typhoid bacilli from the mixture was never in accordance with expectation as judged by viable counts on the original suspensions.

In the fourth paper various observations on colicine production by the author's strains are recorded, without specific reference to the distinction between pathogenic *coli* strains and those used in treatment.

B. Moore

GILLIES, N. E. & ALPER, T. **Reduction in the Lethal Effects of Radiations on *Escherichia coli B* by Treatment with Chloramphenicol.** *Nature.* 1959, Jan. 24, v. 183, 237–8, 3 figs.

Cultures of *Escherichia coli* B were subjected to radiation by X-ray and ultra-violet light; subsequent culture on a solid medium containing 5 μgm./ml. chloramphenicol was found to reduce the lethal effect of these radiations. Stationary phase suspensions were used in the X-ray experiments—it was found that more bacteria survived with chloramphenicol when irradiation took place under anoxic conditions. Similar results were obtained with ultra-violet light, but when logarithmic-phase cultures were used (with UVL), there was a decrease in the number of colonies formed on chloramphenicol plates. With both X-rays and UVL the survival of irradiated *E. coli* could be further increased by culture in nutrient agar before treating with chloramphenicol. It is suggested that chloramphenicol causes the increased survival rates of irradiated organisms by its ability to inhibit protein synthesis [this *Bulletin*, 1958, v. 33, 976]; this process counteracts the metabolic disturbances produced by irradiation.

[See also ALPER and GILLIES, *ibid.*, 1959, v. 34, 81.]

John S. Stevenson

PIRT, S. J. & CALLOW, D. S. **Exocellular Product Formation by Micro-Organisms in Continuous Culture. I. Production of 2 : 3-Butanediol by *Aerobacter aerogenes* in a Single Stage Process.** *J. Applied Bact.* 1958, Dec., v. 21, No. 2, 188–205, 9 figs. [28 refs.]

PIRT, S. J. & CALLOW, D. S. **The Relationship between Maximum Oxygen Solution Rates in a Bacterial Culture and in a Sodium Sulphite Solution under Comparable Aeration Conditions.** *J. Applied Bact.* 1958, Dec., v. 21, No. 2, 206–10, 2 figs. [12 refs.]

POETSCHKE, G. Kinematographische Studien über Bewegungsvorgänge bei Proteus. [**Cinematographic Studies on the Motility of Proteus**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, No. 5/6, 421–31, 15 figs. on 3 pls. [12 refs.]

WILLIAMS, R. E. O. **Epidemic Staphylococci.** *Lancet.* 1959, Jan. 24, 190–95. [66 refs.]

This paper is a review of what is known about the staphylococci which cause epidemics of sepsis in hospitals. It is based on an analysis of 3,803 strains of staphylococci phage-typed at the Staphylococcus Reference Laboratory, Colindale, during 1954–7 and on recent published accounts of 32 outbreaks of infection in maternity hospitals and 15 in surgical units. Full details are given of the phage types of staphylococci concerned in hospital sepsis, and the routes by which staphylococci spread to cause epidemics are discussed.

The most common epidemic types in surgical units were 80, 52A/79, 71, and 7/47/53/54/75 and in maternity units 80, 75/77, and 47/53/75/77. Type 80 was found with increasing frequency during the 4 years 1954–7; 16% of epidemics investigated at Colindale in 1954 were caused by type 80 whereas in 1957 42% were due to this type. The author stresses that although type 80 has become widespread, other types are equally capable of causing epidemics. In hospital outbreaks of infection due to staphylococci of phage group I, including type 80, the epidemic strain was carried by about 25% of the staff, in epidemics due to group II strains by 12·7%, and in outbreaks due to group III strains by 7·7%. The author notes that in many epidemics one individual seemed to introduce the epidemic staphylococcus into the hospital. He considers that in general the dangerous carrier is the person who harbours a strain of a phage type known to be capable of epidemic spread, but he points out that it is very probable that some carriers may be dangerous not only because of the strain they carry but also because they disseminate a particularly large number of staphylococci into their environment.

I. B. R. Duncan

MACCABE, A. F. **Staphylococcal Infection complicating Respiratory Disease.** *Scottish Med. J.* Glasgow. 1959, Feb., v. 4, No. 2, 75–9.

The author studied 50 patients with severe respiratory disease, and staphylococci in the respiratory tract, admitted to 3 hospitals in Edinburgh in the autumn of 1957. In 36 the staphylococcus was clinically important. In 1 hospital, with 26 staphylococcal cases, 2 phage types (53/76/77 and 73) were together responsible for 18 of the infections. In the second hospital, with 20 cases, 11 different types were found. In the third hospital, 3 types were found in 4 patients. The author considered that there was evidence for hospital infection with staphylococci in 12 of the patients in the first hospital, but in only 2 of those in the second, in which infection with a "hospital" type of staphylococcus was commonly associated with a history of previous hospital treatment. In the second hospital, male patients were nursed in 3-bedded rooms, and the bed spacing was 12 feet between centres; infected patients were isolated and barrier nursed. In the hospital with the higher cross-infection rate the patients were nursed in 2 large wards; beds were spaced with 6 feet between centres; and both acute and chronic cases of respiratory disease were admitted.

R. E. O. Williams

ROUNTREE, Phyllis M. & BEARD, Mary A. **Further Observations on Infection with Phage Type 80 Staphylococci in Australia.** *Med. J. Australia.* 1958, Dec. 13, v. 2, No. 24, 789–95. [18 refs.]

The now notorious staphylococcus of phage-type 80, or 80/81, was first recognized by Rountree and her colleagues in Australia in 1954 [this *Bulletin*, 1956, v. 31, 334]; this paper reports the activities of the strain in Australia up to 1957. During the 4 years 1954–7 type 80/81 was the cause of 70 out of 86 epidemics of neonatal infection, and in one Sydney hospital it was isolated from the lesions in 159 of 420 cases of neonatal sepsis. In this hospital 14–19% of the nasal carriers among the staff harboured type 80/81. Of 66 children admitted to hospital with staphylococcal disease, 42 were infected with type 80/81.

Type 80/81 has also been responsible for a substantial part of the staphylococcal sepsis in adults. By 1957, 72% of breast abscesses were due to the type, which also constituted 26% of the antibiotic-resistant staphylococcal infections in in-patients, and 65% of all the septic lesions in the staff of a Sydney hospital. Its increasing frequency as a cause of generalized infection has been discussed elsewhere [*ibid.*, 1959, v. 34, 604].

Most of the strains of type 80/81 isolated in Australia have been resistant to penicillin but sensitive to other antibiotics, though many were also resistant to streptomycin. In this they differ from the epidemic strains of the same phage type found in Britain and the United States, which are usually resistant to tetracycline as well.

Type 80/81 is clearly a strain of high infectivity; whether it is more virulent—in the sense of producing more severe disease—is not clear. The authors speculate on the reason for its biological success and suggest that its penicillin resistance and ability to infect the skin may be of great importance.

[The spread of phage-type 80 in England and Wales has been briefly documented by the reviewer in a paper prepared before the present report was received (*ibid.*, 1959, v. 34, 518).] *R. E. O. Williams*

KOCH, Marie L., LEPLEY, D., Jr., SCHROEDER, C. M. & SMITH, M. B. **Study of Staphylococcic Infections occurring on a Surgical Service.** *J. Amer. Med. Ass.* 1959, Jan. 10, v. 169, No. 2, 99–105. [18 refs.]

The authors report a 1-year study of staphylococcal infection in 2 wards of a surgical service in a Milwaukee hospital. In one ward all patients admitted with, or developing, infection were isolated in rooms with one or two beds, in a section separated from the ward by double doors and provided with separate equipment. Tetracycline drugs were, for a period of 8 months, reserved for use on special request only.

74 patients acquired hospital infections with coagulase-positive "phage typable" staphylococci; 51 were post-operative infections, giving a rate of 4% of the 1,350 operations. [It is not clear whether all staphylococci isolated were submitted to typing; altogether 27% of the strains were untypable.] There was no difference in the incidence in the 2 wards, nor did any change in the prevalence of tetracycline-resistant strains follow the withdrawal of these drugs.

83% of the hospital infections were due to 8 common phage types of staphylococci (53/VA4; 44A; 7; 47/53/54/77/VA4; 77; 47/42D; 80/81 and 3C); these types were also common among strains from admission infections, and among carriers on the staff.

42 of the 74 infections could be related to recognized contacts, mostly among the staff, but 5 were attributed to patient-to-patient spread; 13 of the infections were probably contracted in the operating suite.

The authors stress the importance of seeking faecal as well as nasal carriers of staphylococci [this *Bulletin*, 1956, v. 31, 577], and of typing all the strains isolated. 18 of the cross-infected patients had an average increase in hospital stay of 24 days.

[This paper contains considerable detail that cannot be abstracted; it does not, however, include a summary of the clinical nature of the acquired infections, nor is the evidence for attributing infection to the particular contacts presented.] *R. E. O. Williams*

RAJKOVIC, A. Plazma-agar i Cadness-Graves reakcija u identifikaciji piogenih stafilokoka. **[The Plasma-Agar and Cadness-Graves Test in the Identification of Pyogenic Staphylococci]** *Higijena.* Belgrade. 1958, v. 10, No. 3, 207–18, 1 fig. [22 refs.] English summary.

A modification of the plasma agar test for staphylococcal coagulase has been developed which also enables the presence of fibrinolysin to be detected. The test strain is inoculated deeply into the agar by needle puncture in order to produce a macrocolony. Coagulase is indicated by the development of a halo and fibrinolysin by the subsequent appearance of a ring of clearance which spreads and causes the halo to disappear. By means of the method 112 strains of staphylococcus were examined in parallel with the Cadness-Graves slide test [this *Bulletin*, 1943, v. 18, 870], tube coagulase and fibrinolysin tests. The results of the plasma agar test for coagulase were in complete agreement with the tube tests, coagulase being found in 104 strains by both methods and in 91 by the slide test; the same degree of agreement was found in the fibrinolysin tests. *D. J. Bauer*

WILSON, Elizabeth, FOTER, M. J. & LEWIS, K. H. **A Rapid Test for detecting *Staphylococcus aureus* in Food.** *Applied Microbiol.* Baltimore. 1959, Jan., v. 7, No. 1, 22–6, 2 figs.

For the examination of foodstuffs for *Staphylococcus aureus* the authors recommend the following method. 20 gm. of solid food are blended with 99 ml. of "phosphate dilution water", and 0·5 ml. of the mixture is added to 1·0 ml. brain heart infusion mannitol broth containing 7·5 gm. sodium chloride and incubated, with continuous shaking, at 35°C. for 4–6 hours. A Gram-stained film is examined for cocci and the broth subcultured for a coagulase test, which can be read in 1–3 hours. *Staph. aureus* can thus often be recognized in 7 hours. The method was found capable of yielding positive results in 7–9 hours from an initial inoculum

of 2,000–20,000 cocci. If cultures have to be grown overnight, it is important that they should not be shaken continuously, as this may lead to failure of the coagulase test to give a positive result. *R. E. O. Williams*

STEWARD, Edith E. & KELLY, Florence C. **Variation of Bound Coagulase of** *Staphylococcus aureus*. *J. Bacteriology*. 1959, Jan., v. 77, No. 1, 101–3, 1 fig.

16 strains of coagulase positive staphylococci were tested for bound coagulase by the slide test with bovine fibrinogen and plasma, and for free coagulase by the tube test. The strains were then stored under various conditions for up to 258 days and the tests were repeated on removal from storage and at intervals after repeated subculture.

All strains stored at −26°C. lost their bound coagulase activity while retaining free coagulase activity, as did strains stored in agar and unfrozen cell suspensions. The rate of loss of activity varied with the strain. Lyophilized cultures showed no such loss.

24 serial subcultures failed to restore the bound coagulase activity of 3/9 storage-induced deficient strains but the activity of the other 6 strains was completely or partially restored by subculture. *M. Patricia Jevons*

ROSENBLUM, E. D. & JACKSON, J. L. W. **Mixtures of Coagulase-Positive Staphylococci and Strain Variation in Specimens from Clinical Sources.** *J. Lab. & Clin. Med.* 1959, Feb., v. 53, No. 2, 247–52. [10 refs.]

196 clinical specimens containing coagulase positive staphylococci were plated on Staphylococcus medium 110 and 16 were found to be mixtures of 2 coagulase positive strains on the basis of difference in pigmentation. Individual members of these mixtures were then bacteriophage typed and tested for antibiotic sensitivity. 14 (7%) of the specimens consisted of 2 distinct strains differing in pigmentation, bacteriophage type and sensitivity to antibiotics.

6 of 31 specimens containing strains of type 80/81 from a hospital outbreak contained pigment variants and 4 of these showed some variation in reaction to phages 52, 52A and 44A. *M. Patricia Jevons*

BROWN, D. A., PRICHARD, B. N. C. & QUILLIAM, J. P. **Some Pharmacological Properties of the α-Toxin of** *Staphylococcus pyogenes*. *Brit. J. Pharmacol. & Chemotherapy*. 1959, Mar., v. 14, No. 1, 59–67, 7 figs.

"The α-toxin of *Staphylococcus pyogenes* produced a slowly developing contracture of isolated preparations of rabbit jejunum and of guinea-pig ileum which persisted after thorough washing and left the gut unresponsive to further doses of α-toxin or of acetylcholine. After incubation with antitoxin, the α-toxin no longer produced a contracture. Antitoxin only prevented the α-toxin response if added to the bath fluid before but not after the α-toxin. Certain drugs reduced the α-toxin contracture when added to the bath fluid before or after the α-toxin, but the contracture reappeared on washing. Papaverine abolished the contracture and pethidine was only slightly less active. Mepyramine, amyl nitrite, caffeine, aminophylline, adrenaline and ephedrine partly reduced the contracture. Hexamethonium, cocaine, tubocurarine and gallamine had no effect. The effect of atropine was only small. The gut-stimulant activity/haemolytic unit of two α-toxin samples differed greatly; this difference did not appear to be due to activity of impurities. The implications of these observations are discussed."

WASZ-HÖCKERT, O., KOSUNEN, T. & KOHONEN, J. **Effect of Ethyl Alcohol on the susceptibility of Mice to Staphylococcal Infection. I.** *Ann. Med. Exper. et Biol. Fenniae*. Helsinki. 1958, v. 36, No. 4, 360–65, 3 figs.

Mice were given 8% ethanol in water as drinking fluid and these together with a control group were challenged by intravenous injection of a culture of *Staphylococcus aureus*. A further control group were given 8% ethanol as drinking fluid but were unchallenged. The ethanol did not affect the weight or behaviour of the mice.

13 of 60 mice given ethanol died in 16 days compared with 1 in the control group. None of the unchallenged mice died. Bacterial counts from spleen and kidney showed no difference between the two groups, but counts from the livers of the ethanol group showed a rise after 4 days while those from the control group continued to decline. *M. Patricia Jevons*

ŽMEGAC, Z., ŽMEGAC, Z. J. & BABIC, I. O problemu rezistencije stafilokoka kod piokoknih oboljenja kože. [**The Problem of the Resistance of Staphylococci in Pyogenic Affections of the Skin**] *Radovi Med. Fakul. Zagreb*. 1958, v. 1, 79–92, 4 diagrams. [25 refs.] English summary.

An examination has been made of strains of staphylococci isolated from suppurative skin lesions in 220 dermatological out-patients observed in 1956–7 in Zagreb, Yugoslavia. *Staphylococcus pyogenes* var. *aureus* was isolated in 170 instances (77·3%), *Staph. aureus* in 30 (13·6%), *Staph. pyogenes* var. *albus* in 2 (0·9%) and *Staph. albus* in 18 instances (8·2%). Of the strains of *Staph. pyogenes* var. *aureus* 51·2% were resistant to penicillin, 29·1% to streptomycin, 20·9% to chlortetracycline, 22·1% to oxytetracycline, and only 3·5% were resistant to chloramphenicol; 90·7% were resistant to sulphadiazine. Resistance to 1 antibiotic was present in 33·6%, to 2 in 10·9%, to 3 in 4·6%, to 4 in 11·8% and to 5 in 0·9%. *D. J. Bauer*

LAWRENCE, J. C. **Some Effects of Staphylococcal and Streptococcal Toxins upon Mammalian Skin in Tissue Culture.** *Brit. J. Exper. Path.* 1959, Feb., v. 40, No. 1, 8–14, 2 figs. [19 refs.]

3-day cultures of guineapig or human skin were exposed to staphylococcal α-toxin and to other culture filtrates of staphylococci and streptococci in a respirometer. α-toxin at 100 MHD per ml. caused an immediate increase in respiration followed by a slow decline

and eventual necrosis. Addition of antitoxin within 15 minutes of the addition of toxin greatly reduced the tissue damage; after 60 minutes it had no effect. Culture filtrates containing streptolysin O were slightly toxic when reduced with cysteine; the effect could be eliminated with cholesterol. No effect was demonstrable with streptolysin S. In discussion, it is pointed out that, clinically, streptococcal infection is far more active in killing grafts applied to burns than is staphylococcal infection. *R. E. O. Williams*

HENNINGSON, R. W. **Biochemical Differentiation of Group A and "Human C" Streptococci.** [Correspondence.] *Nature.* 1959, Jan. 17, v. 183, 182.

The author describes a medium for the differentiation of group A from human group C streptococci. This medium consists of a filter-sterilized whey prepared by the addition of rennet to fresh, antibiotic-free raw milk at 40°C. Human group C strains grow in this medium with the production of turbidity. Group A strains do not grow. Results of this test applied to other groups of streptococci are not given.

The author suggests that this test is simpler than Lancefield's serological grouping and more reliable than other methods of differentiation.

[The inhibition of group A strains is interesting since several well authenticated outbreaks of milk-borne disease due to this organism have been reported.]

M. Patricia Jevons

BRUMFITT, W. & MASTERS, P. L. **The Use of Selective Media for the Detection of Beta-Haemolytic Streptococci.** *J. Roy. Army Med. Corps.* 1959, Jan., v. 105, No. 1, 38–41. [12 refs.]

Of 2,000 throat swabs from healthy soldiers, 10% yielded group A streptococci when cultivated on blood agar aerobically and 14% when the blood agar was incubated anaerobically; the use of crystal-violet blood agar incubated aerobically gave a yield of 11%. Aerobic cultures on plain and crystal-violet blood agar of 520 throat swabs from normal children revealed group A streptococci in 13%; the use of the HOLMES and LERMIT [this *Bulletin*, 1955, v. 30, 1021] enrichment medium with subculture on streptomycin-crystal-violet blood agar, in addition to aerobic incubation of blood agar and of crystal-violet blood agar, gave a yield of 22%. *R. E. O. Williams*

WILSON, A. T. **The Relative Importance of the Capsule and the M-Antigen in determining Colony Form of Group A Streptococci.** *J. Exper. Med.* 1959, Mar. 1, v. 109, No. 3, 257–70, 28 figs. on 6 pls. [25 refs.]

A study was made of the colony form of various strains of group A streptococci grown on moist Todd-Hewitt blood agar. 3 forms were recognized: mucoid, matt and glossy. The mucoid form was found always to be associated with capsule formation, as revealed in wet India ink preparations. Streptococci in glossy colonies never had capsules. Matt colonies arise from the collapse of mucoid colonies, which takes place with prolonged incubation even if drying is prevented. No relation could be found between colony form and M-antigen production.

LANCEFIELD and TODD [this *Bulletin*, 1929, v. 4, 554] originally demonstrated an association of the matt colony form and M-antigen production, after TODD (*Brit. J. Exper. Path.*, 1927, v. 8, 289; see also this *Bulletin*, 1928, v. 3, 472) had demonstrated an association with virulence. The association was not very constant and latterly there has been a tendency to use the terms "matt" and "glossy" to signify the presence or absence of M-antigen. Wilson suggests that the symbols M+ and M− should be used for this purpose.

[Wilson's medium allows very good capsule formation; it is possible that on some other media M+ colonies may show a "matt" surface, different from the post-mucoid form discussed in this paper.]

R. E. O. Williams

OBIGER, G. Über die Typisierung von hämolytischen Streptokokken durch den Agglutinations-Test. [**Typing Haemolytic Streptococci by the Agglutination Test**] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 145, No. 5, 439–49. [19 refs.]

This paper reviews briefly the methods of typing group A haemolytic streptococci by slide-agglutination and the preparation of typing sera. The difficulties of obtaining suitably "smooth" suspensions are discussed at some length. The occurrence of cross-reactions is noted [but little is said of the extensive published work attributing them to sharing of T antigens].

R. E. O. Williams

SCHNEWEIS, K. E. & NIKFETRAT, A. Kombinierter Bacitracin- und Hämolyse-Hemmungstest zur praktischen Gruppendifferenzierung hämolysierender Streptokokken. [**Combined Bacitracin- and Haemolysis-Inhibition Test for the practical Group Differentiation of Haemolytic Streptococci**] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 145, No. 5, 450–60. [Numerous refs.]

113 strains of haemolytic streptococci [source not stated] were tested for sensitivity to bacitracin, serological group and for the production of haemolysis on blood agar containing glucose [concentration not given]. Disks containing either 2 or 0·5 units of bacitracin were used, with consonant results All 81 group A strains were bacitracin sensitive, but 11 of 32 strains not group A, including 7 group C strains, were also sensitive. None of the 81 group A strains produced haemolysis on the glucose blood agar, but 7 of the not-A strains also failed. The combination of the 2 tests, however, greatly reduced the risk of misdiagnosing a not-A streptococcus as group A. The incorporation of the dye water-blue in the glucose blood agar was found to assist interpretation.

From each of 100 throat cultures yielding haemolytic streptococci, 8–12 colonies were submitted to the 2 tests; only 2 contained streptococci of more than 1 group.

R. E. O. Williams

ZEMAN, K. & ROTTA, J. Značení beta hemolytických streptokoků radioaktivním fosforem a jejich detekce po experimentální infekci. [**Labelling of Beta-Haemolytic Streptococci with Radio-active Phosphorus and their Detection after Experimental Infection**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1958, v. 7, No. 5, 298–305, 1 fig. English summary (6 lines).

β-Haemolytic streptococci were grown for 15 hours in peptone water containing 400 μc. of ^{32}P as disodium hydrogen phosphate. The organisms were recovered by centrifugation and washed with saline until the washings showed 0·4% of the initial activity; the activity of the bacterial sediment was then 1,006 c.p.m. [counts per minute], or 7·3% of the initial activity. Similar experiments were carried out with Todd and Hewitt broth, ox heart infusion broth alone and with an equal volume of peptone, but the percentage incorporation of radioactive phosphorus by the organisms was in all cases much lower than with growth in peptone water. In further experiments carried out with the latter medium activities of 2,520–3,120 c.p.m. per 10^6 organisms were attained. Mice were infected intranasally with labelled streptococci and the radioactivity of the lungs was determined at intervals up to 6 days; the activity in c.p.m. per 100 mgm. of tissue was somewhat higher than in control mice inoculated with radioactive media without organisms.

D. J. Bauer

SCHWAB, J. H., CROMARTIE, W. J. & ROBERSON, B. S. **Identification of a Toxic Cellular Component of Group A Streptococci as a Complex of Group-Specific C Polysaccharide and a Protein.** *J. Exper. Med.* 1959, Jan. 1, v. 109, No. 1, 43–54, 3 figs. [25 refs.]

Schwab and Cromartie recently showed that injection of a sterile extract of sonically disintegrated group A streptococci intradermally in rabbits produced a chronic multinodular lesion [this *Bulletin*, 1958, v. 33, 392]. The authors have now used ultracentrifugation and electrophoresis to separate the active fraction in the extract and find it to be a protein-polysaccharide complex, the polysaccharide part of which appears to be the group substance. Proteolytic digestion with papain increases the toxic activity of this material, suggesting that it is the polysaccharide that has the specific toxic effect.

R. E. O. Williams

MESROBEANU, Lydia, BALDOVIN, Coralia, MIHALCO, Florica & MITRICA, Natalia. Purification et concentration de la streptolysine "O" par l'acide trichloracétique. [**The Purification and Concentration of Streptolysin O by means of Trichloracetic Acid**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, June, v. 17, No. 2, 251–4.

A suitable streptococcus is grown in a buffered glucose broth for 18 hours. The culture is then spun; the supernatant fluid is cooled to 4°C. and concentrated trichloracetic acid is added to bring the *p*H to 3·5. After 10 minutes the precipitate is spun out and redissolved in N/200 sodium bicarbonate, 1/10th the volume of the original culture. The *p*H is brought to 7·8 and the preparation filtered through a Seitz pad and stored in fluid or desiccated form at room temperature or at 4°C. In all cases it was found to be stable for up to 8 months. The final preparation had 160 combining units per ml.

R. E. O. Williams

KUSAMA, H.; OHASHI, M.; SHIMAZAKI, H.; FUKUMI, H. **Studies on Streptolysin O and Antistreptolysin O. I. Spectrophotometric Determination of the Hemolytic Activity of Streptolysin O by the Fifty per cent End-Point Titration** [KUSAMA, OHASHI, SHIMAZAKI & FUKUMI]. *Japanese J. Med. Sci. & Biol.* 1958, Oct., v. 11, No. 5, 347–57, 6 figs. [13 refs.] **II. Neutralization Reaction of Streptolysin O by Antistreptolysin O** [KUSAMA, OHASHI, SHIMAZAKI & FUKUMI]. *Ibid.*, 359–73, 6 figs. [12 refs.] **III. A Practical Method for the Antistreptolysin O Titration of Human Sera** [KUSAMA]. *Ibid.*, 375–82, 1 fig. [10 refs.]

KOROBKOVA, E. I. **Action of Glycine on *Pasteurella pestis*—III. The Nature of Plague Toxin and its Importance in Active Immunization.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1662–7. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 718.]

REYN, Alice, KORNER, B. & BENTZON, M. W. **Effects of Penicillin, Streptomycin, and Tetracycline on *N. gonorrhoeae* isolated in 1944 and in 1957.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 227–39, 4 figs. [Numerous refs.]

This study carried out at the State Serum Institute, Copenhagen, concerns 90 strains of gonococci isolated in 1944, 103 isolated routinely in 1957, and 103 submitted in 1957 with a request for a sensitivity determination. Sensitivity to penicillin, streptomycin and tetracycline was determined by several methods, including a plate dilution method, which was preferred and on the results of which conclusions are mainly based.

Penicillin. The 1944 strains showed only a 6-fold variation in degree of sensitivity about a norm of 0·01 μgm./ml. The more recent ones included strains inhibited only by concentrations of about 0·2 μgm./ml.: these were more numerous, and the total range greater (180-fold compared with 80-fold) among the strains submitted with a request for a sensitivity test.

Streptomycin. 4 recent strains, all from cases treated with this antibiotic, were highly resistant: otherwise the 1944 and 1957 strains showed closely similar degrees and ranges of sensitivity.

Tetracycline. There was little difference between the groups, except a rather wider range in the latter ones.

Analysis of the findings gave some indications that resistance to one antibiotic is liable to be accompanied by a lesser degree of sensitivity to another.

Therapeutic policy is discussed in view of these findings and larger doses of penicillin are advocated. The use of streptomycin is contra-indicated because a high

degree of resistance may develop. The use of long-acting penicillin preparations for prophylaxis is deprecated, since these may have some responsibility for the development of resistance. *L. P. Garrod*

PILLOT, J. & FAURE, M. Composition antigénique des tréponèmes. I. L'antigène protéique de groupe de la souche Reiter. [**The Antigenic Constitution of *Treponema*. I. The Protein Antigen of Reiter's Strain**] *Ann. Inst. Pasteur.* 1959, Feb., v. 96, No. 2, 196–210.

This long and highly technical article describes the preparation of an antigen from the Reiter spirochaete which is essentially protein in nature. This substance is closely bound to the body of the spirochaete.

The technique of the test is similar to that of the Kolmer WR; spirochaetes were cultured in the usual way, washed and subjected to various methods of breaking them up, shaking, alkalinization, delipidation; the most effective method is submission to supersonic waves which breaks up the bodies of the spirochaetes; a *p*H above 12 results in solution of the spirochaetes but the protein antigen loses its activity. Delipidation, by means of butanol, breaks up the various cellular constituents and liberates numerous soluble substances.

Purification is carried out with ammonium sulphate, alcohol or acetone, or acids.

The technique of preparation of the antigen is a highly complicated procedure set out in detail; for this the original should be consulted. Purified antigen contains 12% nitrogen and 1·96% phosphorus, is used in a dilution of 1/100 to 1/150 and is not anti-complementary; it is very similar to that in *Treponema pallidum* and does not react with "reagin"; it is essentially multiple.

The antigen remains active if kept at *p*H 7·2–7·4 with phosphate or veronal with the addition of glycerin.

It is of interest to note that purified antigen does not seem to be better than non-purified antigen (spirochaetes submitted to supersonic waves).

This antigen detects yaws as well as syphilis.

T. E. Osmond

HEYMANN, G. & SIEFERT, G. Experimentelle Untersuchungen über Spirochaeten-Antigene. I. Mitteilung. Biochemische Analyse der Struktur-Elemente verschiedener Spirochaeten. [**Investigations on Spirochaetal Antigens**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, Sept., v. 116, No. 3, 257–75, 6 figs. [48 refs.]

The English summary appended to the paper is as follows:—

"The protein-bound and free amino acids of different spirochaetal species (Treponema pallidum, Reiter's spirochaeta, Leptospira biflexa) were examined. The high content of acid protein-bound amino acids (30%) seems to be characteristic for the spirochaetal protein. The DNA/RNA ratio corresponds to that of the bacteria. DNA is chiefly localized in the cytoplasma, RNA as well in the cytoplasma as in the supporting organella.

"The lipid content of 20% exceeds by far that of the bacteria.

"The enzymatic digestion of spirochaetes shows two separated stages which are represented by the gradual destruction of the cytoplasma on the one hand and of the axial rod and the fibrillae on the other hand."

SIEFERT, G. & STEIGER, I. Experimentelle Untersuchungen über Spirochäten-Antigen. II. Mitteilung. Isolierung und Charakterisierung einer serologisch aktiven Eiweissfraktion aus *Treponema pallidum*. [**Experimental Investigations on Spirochaete-Antigens. II. Communication. Isolation and Characteristics of an Active Protein Fraction from *Treponema pallidum***] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Feb., v. 117, No. 2, 147–55, 2 figs. [19 refs.]

The material used in this investigation was a carefully washed suspension of treponemata (strain Nichol) prepared from the infected testicle of a rabbit.

After removal of lipoid with acetone the residual spirochaete sediment was disintegrated by repeated freezing and thawing in a 0·2% solution of desoxycholic acid in 0·2M solution of Na citrate.

The examination of the protein fraction obtained was carried out by ultra-violet absorption and indicated presence of albumin but not of nucleic acid, and electrophoresis on paper developed with "Amidoschwarz 10B" provided evidence of the presence of at least 4 compounds in varying concentrations.

The most important observation was that this preparation gave active complement fixation with immune animal sera and remained active with serum from which syphilitic "reagin" had been removed by absorption. The same absorption removed all reaction between the serum and a cardiolipin antigen.

J. W. McLeod

HORNE, T., TURNER, G. C. & WILLIS, A. T. **Inactivation of Spores of *Bacillus anthracis* by γ-Radiation.** [Correspondence.] *Nature.* 1959, Feb. 14, v. 183, 475–6.

Co 60 was used as source of gamma radiation and tested on packed goat hair contaminated with spored cultures of *Bacillus anthracis* of which 8 separate strains were used including 2 recently isolated by Prof. D. T. ROBINSON of Liverpool.

The range of resistance was a narrow one. No strain yielded spores which resisted $1{\cdot}5 \times 10^6$ rad and the most sensitive was killed by $1{\cdot}0 \times 10^6$ rad.

It is expected that $2{\cdot}0 \times 10^6$ rad would give an adequate margin in the use of this method for industrial purposes. *J. W. McLeod*

FULTHORPE, A. J. **Estimation of Tetanus Toxoid by Different Methods, including Haemagglutination Inhibition.** *Immunology.* Oxford. 1958, Oct., v. 1, No. 4, 365–72, 5 figs.

The author's proposed modification of STAVITSKY's method [this *Bulletin*, 1954, v. 29, 1204] of determining the titre of an antitoxin by its capacity to agglutinate

sheep red cells has already been reviewed [*ibid.*, 1958, v. 33, 73]. It consists in determining the largest amount of toxoid which is just insufficient to prevent the agglutination of toxoid-coated red cells which are submitted to the action of graded mixtures of toxoid with a standard amount of antitoxin.

Working with tetanus toxin, toxoid and antitoxin, the author made a comparison between the titrations of toxoid determined (a) by the standard flocculation method, (b) the *in vivo* total combining power and (c) his own haemagglutination inhibition test as described above.

The *in vivo* test consists in determining the least amount of toxoid which, when mixed with 2 units of antitoxin, leaves insufficient to protect mice from 1 unit of toxin added subsequently to the mixture.

When these three methods are compared with a variety of toxoid preparations, *i.e.* those from crude culture filtrates, from separated and autolysed bacteria and from highly purified toxoids, and from such products prepared with varying concentrations of formaldehyde, it is found that the discrepancies between tests (a) and (b) are considerably greater than between tests (b) and (c). These differences are attributed to two factors: (a) the presence in crude filtrates of flocculating antigens distinct from specific toxin, and (b) a denaturing effect of formaldehyde on the specific toxin which is more marked in the more purified products and affects the specific toxin more than the subsidiary flocculating antigens. There is here general support of the conclusions of POPE and STEVENS [this *Bulletin*, 1958, v. 33, 877] with regard to the complexity of apparently pure toxin preparations.

The practical recommendation is made that in view of this denaturing action of formaldehyde on toxoid, that substance should be removed at the end of the period necessary for "toxoiding". *J. W. McLeod*

IAKOVLEV, A. M. **The Importance of Antitoxic Immunity for the Defence of the Body in Respiratory Penetration by Bacterial Toxins—I. Rôle of Passive Immunity in the Defence of the Body against Respiratory Disease caused by *Clostridium botulinum* Toxins.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 6, 904–9, 5 figs. [Translated from Russian.]

In this investigation the lethal effect of *Clostridium botulinum* toxin on mice and guineapigs when administered by the respiratory tract was examined. The animals were kept in a closed chamber in which the toxin was inhaled as a suspension of fine droplets from an "atomized" solution.

From these observations it appeared that the toxin was particularly lethal to animals when inhaled in this way and that although protection could be obtained with serum given as a prophylactic or up to 10 hours after exposure to infection, the duration of protection was less than if inoculation of the poison was by other routes. The protection was specific as between A and B toxin. [The circumstances in which animals might be exposed to the inhalation of *botulinum* toxin are not discussed.] *J. W. McLeod*

FUNGI

KNIGHT, R. A., HILL, G. & MARCUS, S. **Immunization of Mice with Polysaccharides of *Histoplasma capsulatum*.** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 356–8. [13 refs.]

"*H. capsulatum* strain G17(M) polysaccharide was capable of producing active resistance against intravenously induced histoplasmosis in mice. However, mice immunized with a *H. capsulatum* whole yeast cell antigen showed greater resistance when the *H. capsulatum* polysaccharide immunized, whole cell immunized and nonimmunized control mice were challenged by the intravenous injection of known numbers of viable *H. capsulatum* yeast phase organism."

RICKETTSIAE

WEISS, E., DRESSLER, H. R. & SUITOR, E. C., Jr. **Further Studies of Drug-Resistant Strains of *Rickettsia prowazekii*.** *J. Bacteriology.* 1959, Jan., v. 77, No. 1, 91–100, 6 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 707.]

BALAEVA, N. M. **The Biological Properties of *Rickettsia mooseri* after Prolonged Cultivation in the Intestine of the Body Louse. III. The Morphology of *Rickettsia mooseri* and *R. prowazeki* studied by means of the Electron Microscope.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 7, 1147–8. [Translated from Russian.]

COHN, Z. A., BOZEMAN, F. Marilyn, CAMPBELL, Janis M., HUMPHRIES, J. W. & SAWYER, T. K. **Study on Growth of Rickettsiae. V. Penetration of *Rickettsia tsutsugamushi* into Mammalian Cells *in vitro*.** *J. Exper. Med.* 1959, Mar. 1, v. 109, No. 3, 271–92, 4 figs. [26 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 708.]

ZDRODOVSKII, P. F. & GOLINEVICH, E. M. **Differentiation of the Causative Organism of East African Tick-Borne Rickettsiosis (Kenya Tick Typhus) and Indian Tick-Borne Rickettsiosis (Indian Tick Typhus).** *Problems of Virology.* London. 1958, v. 3, No. 4, 219–23. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 708.]

ROBERTS, Audrey N. & DOWNS, Cora M. **Study on the Growth of *Coxiella burnetii* in the L Strain Mouse Fibroblast and the Chick Fibroblast.** *J. Bacteriology.* 1959, Feb., v. 77, No. 2, 194–204, 5 figs. [19 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 709.]

KORDOVÁ, N. **Filterable Particles of *Coxiella burneti.*** *Acta Virologica.* Prague. 1959, Jan., v. 3, No. 1, 25–36, 1 text fig. & 8 figs. on 2 pls. [19 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 710.]

MORELJ, M. & GERBEC, M. **Immunological Analysis of some Strains of *Coxiella burneti.*** *Acta Virologica.* Prague. 1959, Jan., v. 3, No. 1, 37–45, 5 figs. [18 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 710.]

SOKOLOVA, N. F. & FEDOROVA, N. I. **A Further Study of the Resistance of *Rickettsia burneti* to the Action of Certain Chemical Substances.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1264–7. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 711.]

KULAGIN, S. M., SOKOLOVA, N. F. & FEDOROVA, N. I. **A Study of the Disinfection of Surfaces infected with the Causative Agent of Q Fever.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1271–5. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 711.]

KULAGIN, S. M., SOKOLOVA, N. F., SUBBOTIN, A. A. & SILICH, V. A. **The Study of Disinfection of Underclothes, Overalls and Articles in Cases of Q Fever.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1275–9. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 711.]

BACTERIOPHAGES

KUBINSKI, H. **Investigations on the Adsorption of Phage I Vi to the Cells of *Salmonella typhi.* I.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 2, 57–61, 2 figs. [13 refs.]

"During investigations on the adsorption kinetics of phage I *Vi* to cells of *Salmonella typhi* of the strain *A*, it was established that, in some cases, the adsorption is very weak (very flat adsorption curve) or that a period of adsorption of the phage to the cell lasting ca. 3 min. is followed by elution of the virus into the surrounding liquid. The viruses which react in this manner are, as a rule, young and freshly cultured. Such factors as time and temperature change the type of adsorption to a continuous one. The probable mechanism of this phenomenon is discussed."

KUBINSKI, H. **Influence of Substrate on the Curve of Adsorption of Bacterial Viruses to Cells. II.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 2, 63–8, 4 figs.

"The phenomenon of transition of one phase (PnEl) of the phage I *Vi* into another (PEl) under the influence of native eluate obtained from *Salmonella typhi A* cells is described. This reaction is expressed by the change of the character of the curve of adsorption of the phage to the cell. It is demonstrated that the antigen *Vi*, i.e. the substrate of the phage I enzyme is essential to the reaction of the PnEl—PEl transition. This reaction, however, cannot take place solely under the influence of pure antigen *Vi*, but can occur only in the presence of a substance of a co-factor type, which is little known as yet and provisionally called factor *X*. The changes occurring in the virus protein are totally reversible and may pass in both directions practically an infinite number of times. Each phage I *Vi*, if infectious in the PnEl phase, may be transformed to the PEl phase by the action of the complex antigen *Vi* + factor *X*."

ENTNER, N. & ENGELSBERG, E. **An Effect of Glucose on Bacteriophage Synthesis in *Salmonella typhi-murium.*** [Correspondence.] *Nature.* 1958, Dec. 27, v. 182, 1808–9, 1 fig.

Wild type *Salmonella typhi-murium* induced to form an adaptive enzyme by a given substrate is inhibited from producing the enzyme by glucose. A mutant has been obtained, however, which, in the presence of substrate, continued to produce the enzyme when glucose was added. This "diauxie-resistant" mutant was found to contain 3 times as much glucose-6-phosphatase as the wild type.

Infection of wild type *Salm. typhi-murium* with phage P22 was followed by lysis in the absence of glucose, but by lysogeny if glucose was added to the culture just before infection. In contrast, infection of the mutant was invariably followed by lysis, whether or not glucose was added.

The authors suggest that it is possible that during protein synthesis glucose competes with the phage chromosome for the phosphate-nucleotide pool. The results would be explained therefore if glucose has the greater affinity for the pool and consequently inhibits the synthesis of phage protein (as it does adaptive enzyme protein) in the wild type cell. Lysogeny is established because no protein synthesis is available for the phage vegetative cycle. It is suggested that protein synthesis allowing phage multiplication (or adaptive enzyme formation) can occur in the mutant because

the phosphate-nucleotide pool is quickly regenerated by the large amounts of glucose-6-phosphatase in the cell.

Janice Taverne

DÉNES, G. & POLGÁR, L. **T2 Phage Infection of "Protoplasts" obtained by Penicillin Treatment of** *Escherichia coli B.* [Correspondence.] *Nature.* 1959, Mar. 7, v. 183, 696–7, 1 fig. [10 refs.]

It was noticed that synthesis of the adaptive enzyme β-galactosidase in *Escherichia coli* B protoplasts made by treatment with penicillin stopped on addition of phage T2. Phage infection of the protoplasts was therefore investigated. Intact cells and protoplasts were lysed prematurely at intervals after infection with T2, and the infective phage measured; phage synthesis was found to proceed at the same rate in both systems.

It is argued that phage receptors residing in the bacterial cell wall must therefore be unchanged in protoplasts, and as penicillin is supposed to inhibit the synthesis of the mucopolysaccharide component of the cell wall only [this *Bulletin*, 1957, v. 32, 686; 1958, v. 33, 1071], then T2 phage receptors must be bound to the lipo protein part of the cell wall.

Janice Taverne

NUTTER, R. L. & SINSHEIMER, R. L. **Studies upon DNA Synthesis during Multiplicity Reactivation of T2r+ Bacteriophage.** *Virology.* New York. 1959, Mar., v. 7, No. 3, 276–90, 6 figs. [20 refs.]

ASTRACHAN, L. & VOLKIN, E. **Effects of Chloramphenicol on Ribonucleic Acid Metabolism in T2-Infected** *Escherichia coli. Biochim. et Biophys. Acta.* 1959, Apr., v. 32, No. 2, 449–56, 4 figs. [21 refs.]

DUKES, P. P. & KOZLOFF, L. M. **Phosphatases in Bacteriophages T2, T4, and T5.** *J. Biol. Chem.* 1959, Mar., v. 234, No. 3, 534–8, 1 fig. [22 refs.]

BERTANI, L. Elizabeth. **The Effect of Ultraviolet Light on the Establishment of Lysogeny.** *Virology.* New York. 1959, Jan.. v. 7, No. 1, 92–111, 10 figs. [13 refs.]

Cells of *Shigella dysenteriae* infected with phage P2 or with some of its temperate or virulent mutants were irradiated with UV light at intervals after infection and the survivors measured by plaque formation (lytic complexes) or by ability to form lysogenic colonies (lysogenic complexes). UV resistance increased rapidly in both cases, but earlier with virulent than with temperate phages. The UV resistance of lysogenizing complexes decreased towards the end of the latent period. It was found that the frequency of lysogeny increased if infected cells were irradiated at a critical time in the early part of the latent period, *i.e.* 10–15 minutes after infection.

The author discusses 2 possible explanations of this finding: (1) If the establishment of lysogeny requires a step involving recombination, then because UV irradiation has a stimulating effect on recombination it would also increase the frequency of lysogenization. (2) If the phage DNA concerned with protein synthesis plays a part which is completed halfway through the latent period and early UV irradiation disturbs this activity, then lysogeny would be favoured because substances causing inhibition of protein synthesis have been shown to increase the frequency of lysogenization [Bertani, this *Bulletin*, 1957, v. 32, 1186].

Janice Taverne

COHEN, Denise. **A Variant of Phage P2 originating in** *Escherichia coli*, **Strain B.** *Virology.* New York. 1959, Jan., v. 7, No. 1, 112–26, 2 figs. [25 refs.]

A variant of a virulent P2 phage grown in *Escherichia coli* B was found to be *dismune*; *i.e.* bacteria lysogenized by it did not become immune to infection with wild type P2, and *vice versa.* The variant, P2 *Hy dis* (for "hybrid dismune") was inactivated by antiserum and by UV at the same rate as wild type P2 and its mutants, but differed from the phage it was derived from in being temperate, sensitive to heat, and in producing small plaques. In addition, although originally grown on *E. coli* B, it could not form plaques on this strain; it adsorbed to the bacteria but did not kill them.

As it seemed unlikely that all these new properties had arisen in P2 *Hy dis* by a one-step mutation, it was postulated that, as a rare event, recombination occurred between the P2 virulent phage and a hypothetical prophage of *E. coli* B. This would also explain the immunity of *E. coli* B to P2 *Hy dis.*

In support of this theory it was found that dismune phages appeared when other strains of P2 differing in virulence were grown in *E. coli* B, and that none were observed when P2 was grown in *Shigella dysenteriae.* In a single burst experiment, dismune phages were distributed among lysing cells in the manner expected of rare recombination events. *E. coli* B could be "cured" of its prophage, either by UV irradiation or by superinfection with P2. The cured strain had lost its immunity to P2 *Hy dis* and was no longer able to give rise to dismune variants upon infection with P2.

The presumptive evidence for the existence of a prophage in *E. coli* B is thus very strong. However, no direct proof was obtained. Free phage was never detected and the prophage was not induced by UV. The possibility that this particular prophage was necessary for host controlled variation of P2 grown in *E. coli* B was excluded. It seemed likely that the prophage was defective. Attempts to demonstrate this were unsuccessful.

Janice Taverne

KELEMEN, G. **Genetic Transduction in the** *Salmonella* **Group.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 4, 383–8, 1 fig. [13 refs.]

This paper reports the results of some transduction experiments done with 3 phages isolated from different salmonella strains, and with Lederberg's PLT 22 phage. The recipient O strain and phage lysate were cultured on one arm of a U-tube containing semi-solid agar, and motile organisms having the transduced character were picked from the other arm. Phages from *Salm. enteritidis* and Salm. Essen were found to transduce the

flagellar antigen *gm* to the O form of *Salm. paratyphi B*. A phage from *Salm. paratyphi A* transduced flagellar antigen *a* to *Salm. enteritidis*. Phage PL 22 transduced flagellar antigen *i* to *Salm. paratyphi B*. In each case the recipient strains acquiring the transduced flagellar antigens retained their original fermentation reactions, mouse pathogenicity and slime wall-forming properties. *Janice Taverne*

TESSMAN, I. **Some Unusual Properties of the Nucleic Acid in Bacteriophages S13 and X174.** *Virology.* New York. 1959, Mar., v. 7, No. 3, 263–75, 3 figs. [17 refs.]

POSPELOVA, V. V. **The Biological Features of Diphtheria Bacteriophages—I. Isolation of the Phage from Patients. Range of Action and Resistance of the Phage to Inactivating Agents.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 6, 883–8. [23 refs.] [Translated from Russian.]

Phage active on *Corynebacterium diphtheriae* was isolated from pharyngeal washings from 2 out of 23 patients with diphtheria. Both were toxic cases from whom the *gravis* strain was isolated, and phage was not detected until the patients started to recover. This confirms the results of other Russian workers who also isolated phage only from severe cases of diphtheria at the time of recovery.

Some experiments with diphtheria phages are described. 43 strains of *C. diphtheriae* were tested for sensitivity to 5 different phages. *Gravis* strains appeared to be more sensitive than *mitis* strains, and no connexion was observed between the sensitivity pattern and toxigenicity. The inactivation of the phages by acid, by heating and UV-irradiation is described. One phage strain was observed to be more thermostable and more UV-resistant than the rest.

Janice Taverne

WHITE, A. C., FOSTER, Frances & KNIGHT, V. **Propagation of Staphylococcal Phages in Liquid Medium.** *Antibiotics & Chemotherapy.* New York. 1959, Feb., v. 9, No. 2, 81–6, 1 fig.

Suspensions of 24 staphylococcal typing phages prepared by growing them overnight at 30°C. on propagating strains in heart infusion broth containing calcium at a concentration of 0·004 M per litre ("from a molar solution of U.S.P. hydrous calcium chloride prepared in distilled water and sterilized by autoclaving"), and then kept at room temperature for 24 hours, had titres and specificity of action equivalent to those of phage suspensions obtained by propagation in semi-solid agar.

R. S. F. Hennessey

PARNAS, J. & BULIKOWSKI, W. Résultats de recherches antérieures sur les phages propres anti-brucella (2e communication). [**Studies on Anti-Brucella Phage. Second Communication**] *Arch. Inst. Pasteur de Tunis.* 1958, Sept.–Dec., v. 35, Nos. 3/4, 315–26, 2 figs. [12 refs.]

This paper describes, in more detail, results already published in *Bull. Acad. Polonaise des Sci.*, 1958, v. 6, 201 [this *Bulletin*, 1958, v. 33, 1180] and in *Nature*, 1958, v. 182, 1610 [*ibid.*, 1959, v. 34 (392)], on the isolation of some phages from type cultures of *Brucella*. In contrast to the earlier report, further work has shown that some strains of phage lysed *Br. melitensis* and *Br. suis*. *Janice Taverne*

IVÁNOVICS, G. & LANTOS, J. **An Effective Method for Isolation of Anthrax Phages.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 4, 405–10, 4 figs.

Anthrax phages were isolated from soil by incubating samples in broth, to allow spore germination and the release of any carried phages, and then adding streptomycin and a streptomycin-resistant Davis strain of *Bacillus anthracis*. Thus the growth of contaminants was inhibited while *B. anthracis* acted as host to any specific phages present, which were later isolated by plating on the streptomycin-resistant indicator.

Phages of 5 different plaque types were isolated in this way from 10 out of 13 soil samples. They were specific for *B. anthracis* (the sensitivity patterns of 10 *anthracis* strains were tested) and had little or no effect on *B. cereus* strains. They did not attack bacteria from any other genera, or *B. megaterium* or *B. subtilis*. These phages have therefore a host range resembling that of the anthrax phage isolated from *B. cereus* strain W by MCCLOY [this *Bulletin*, 1951, v. 26, 1217].

Janice Taverne

JEENER, R. **The Action of Ribonuclease on Sensitive and Non-Induced Lysogenic Cells of** *Bacillus megaterium*. *Biochim. et Biophys. Acta.* 1959, Mar., v. 32, No. 1, 99–105, 4 figs. [14 refs.]

High concentrations of ribonuclease (RNase) lyse cells of *Bacillus megaterium* instantly, whether or not they are lysogenic. At lower RNase concentrations, growth of both strains was found to slow down, only the lysogenic strain lysing 30–120 minutes later. This interval was constant for the strain and independent of RNase concentration below 100 μgm./ml. Lysis did not occur at 30°C. Cells surviving high concentrations of RNase gave rise to descendants having a stable, hereditary resistance to the enzyme.

In conditions in which lysis did not occur, RNase reduced both the bacterial growth rate and the viable count. Although cell respiration, the ratios of RNA and DNA to cell protein and the uptake of ^{14}C-labelled adenine were all normal, the decrease in protein synthesis was accompanied by a change in the base ratios of the RNA, there being a 10% increase in uridylic acid in cells grown in the presence of RNase.

Thus RNase did not cause a breakdown in cell structure and the bacterial division rate was more affected than the synthesis of cell constituents. The author suggests 2 ways in which RNase might have this effect. (1) If there was a preferential breakdown of RNA assembled after addition of the enzyme, then the rate of accumulation of RNA would slow down although the ratio of uptake of ^{14}C-labelled adenine to net synthesis would not change. (2) If RNase altered the structure of RNA molecules so that they could not act

as templates in protein synthesis, then growth would slow down while no breakdown of RNA would be observed. *Janice Taverne*

JEENER, R. **The Action of Ribonuclease on Phage Protein Synthesis by an Induced Lysogenic *Bacillus megaterium* Culture.** *Biochim. et Biophys. Acta.* 1959, Mar., v. 32, No. 1, 106–16, 5 figs. [28 refs.]

RNase (in a concentration which did not lyse the cells) inhibited the synthesis of phage protein in a lysogenic culture of *Bacillus megaterium* induced with UV light, but did not stop cell growth. The synthesis of phage protein (measured after precipitation with antiserum) was completely inhibited if RNase was added before or immediately after induction. When RNase was added at different times during the latent period the inhibition decreased with time in such a way as to suggest that it impaired the function of a mechanism being built up throughout the time of protein synthesis rather than of an existing mechanism. The number of infectious phage particles produced depended upon the amount of phage protein already synthesized before RNase was added. It seemed, therefore, that phage protein made in the presence of small amounts of RNase was abnormal. It was, however, assembled into complete particles visible in electron micrographs and their lack of infectivity was due to a failure in adsorption.

The author supposes that RNase modifies the structure of RNA molecules acting as templates in phage protein synthesis. The synthesis of phage protein would be inhibited to a greater extent than that of bacterial protein if newly synthesized phage RNA were more accessible to RNase than bacterial RNA enclosed in cell structures already existing at the time of induction, or if RNase alters only RNA synthesized in its presence. *Janice Taverne*

VIRUSES

In this section the abstracts are arranged as far as possible in the following order: General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; Others.

KABANOVA, E. A., MASTYUKOVA, Y. N. & PISHCHURINA, M. M. **Studies on Vaccinia Virus Multiplication in Rabbit Cornea Epithelial Cells using Fluorescent Antibodies.** *Acta Virologica.* Prague. 1958, Oct.–Dec., v. 2, No. 4, 250–52. [12 refs.]

Using the fluorescent antibody method developed by COONS the authors demonstrated vaccinia virus antigens in rabbit corneal cells 48 hours after the animals' eyes had been scratched and virus rubbed in. Potent virus preparations infected nearly all the available corneal cells; a weaker preparation was not as effective.

[Similar findings were reported for vaccinia-infected human cells in culture by NOYES and WATSON (this *Bulletin*, 1956, v. 31, 87).] *Colin Kaplan*

SHIN-JUNE, U-WEY-HUANG, TSYAN-SUE-SHAN. **Contribution to the Mechanism and Control of Post-Vaccination Immunity of White Mice in Tick-Borne Encephalitis.** *Acta Virologica.* Prague. 1958, Oct.–Dec., v. 2, No. 4, 235–44. [11 refs.]

Mice immunized with 6 doses of formalinized Russian spring-summer vaccine had protection indices of at least 100,000 LD50 when challenged intraperitoneally or subcutaneously but no protection against intracerebral challenge. Nor was protection against intracerebral challenge conferred by 2 doses of vaccine followed by 3 doses of live virus. 2 groups of mice with protection indices of at least 100,000 had serum neutralizing indices of 30 and 16 and their brain-tissue (largely freed of blood) contained no antibody. Mice given antiserum intraperitoneally on one side and virus on the other were protected in spite of the inoculation of irritants intracerebrally. But antiserum given intraperitoneally gave no protection against intracerebral challenge.

Immune and susceptible mice inoculated intracerebrally had the same amounts of virus in their brains from 1 day after inoculation until death: the susceptible mice had viraemia throughout but the immune mice only terminally. Immune and susceptible mice infected intranasally both had virus in the brain from the 3rd day onwards; viraemia occurred for 1 day only in the immunes but persisted from the 5th day onwards in the susceptibles. Invasion of the brain from the nose therefore appears to be *via* the olfactory nerves and not the blood stream. Immune and susceptible animals were also inoculated intraperitoneally. Virtually no viraemia was detected and invasion of the brain by virus was detected only where very large doses of virus had been given and then only at the 7th day after inoculation. *C. E. Gordon Smith*

BIEGELEISEN, J. Z., Jr., SCOTT, L. V. & LEWIS, V., Jr. **Rapid Diagnosis of Herpes Simplex Virus Infections with Fluorescent Antibody.** *Science.* 1959, Mar. 6, v. 129, 640–41.

A method has been developed for the rapid detection of herpes virus in smears of pathological materials by means of the fluorescent antibody technique. Antiserum was prepared by immunizing rabbits with chick embryo fluids containing herpes virus, and was absorbed with dried mouse liver powder to remove unspecific fluorescing material and then conjugated with fluorescein isocyanate. Smears were prepared from scrapings of vesicles obtained from 13 patients suffering from vesicular skin eruptions, a nasal swab from a patient suffering from acute herpetic stomatitis and a specimen of cerebrospinal fluid from a patient suffering from non-bacterial meningitis. The smears were fixed in acetone for 10 minutes, washed in saline and stained with fluorescent antiserum. Specific fluorescence was observed in 7 vesicle smears and the nasal smear, and herpes virus was subsequently isolated on the chorio-allantoic membrane from materials from the same patients. No specific fluorescence was observed in the remaining 7 preparations, and attempts to isolate virus from the patients concerned were also unsuccessful. *D. J. Bauer*

FARNHAM, Ann E. **The Formation of Microscopic Plaques by Herpes Simplex Virus in HeLa Cells.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 317–27, 5 figs. [15 refs.]

In HeLa cell cultures infected with herpes virus plaque-like foci of infection appeared after 2–3 days and were easily visible under the microscope used for routine examination of the cultures. Secondary plaques caused by dissemination of virus in the culture fluid appeared after 4–5 days; their appearance could be prevented by adding specific antiserum to the cultures after 48 hours, and the plaque count then remained constant. A reliable count could be made without the addition of antiserum if it was carried out on the 3rd day. The plaque count was dependent on the volume of the virus inoculum, and with a constant dose of virus an inoculum of 0·1 cc. gave 1·7 times as many plaques as an inoculum of 1 cc. Removal of the inoculum at various times after infection and subsequent counting of the plaques showed that 50% of the virus was adsorbed by the cells after 50 minutes. The plaque count was proportional to the logarithm of the virus concentration over at least 1·2 log units, and in counts of 50 replicate cultures the distribution was Poissonian. In comparative titrations in HeLa cell cultures and on the chorio-allantoic membrane the ratio of pock units to plaque-forming units ranged from 2 to 13.

D. J. Bauer

STOKER, M. G. P. **Mode of Intercellular Transfer of Herpes Virus.** [Correspondence.] *Nature.* 1958, Nov. 29, v. 182, 1525–6.

HeLa cells infected with the HFEM strain of herpes virus in a multiplicity of 0·44–0·78 plaque-forming unit per cell and containing virus in the lag phase of growth were resuspended and deposited on monolayers of uninfected HeLa cells; 43·6% of the infected cells gave rise to plaques, although only 7·7% formed pocks on the chorio-allantois, which is known to be 10 times as sensitive as HeLa cells for the detection of infective herpes virus. When the cells were disrupted by freezing less than 2% formed plaques. In further experiments with the same dose of virus and conditions of infection none of 30 cells released virus infective for HeLa cells when isolated in single drops, and only 3 of 80 released virus detectable on the chorio-allantois. Plaques could also be found when infected cells were deposited on monolayers in the presence of a high concentration of antiserum.

These findings suggest that plaque formation is not brought about by the spread of infective virus. The herpes plaque in its early stages consists of a syncytium formed by cell fusion, and it is suggested that the mass becomes infected by the intracytoplasmic transfer of virus in a vegetative or non-infective state.

[See also this *Bulletin*, 1959, v. 34, 175.]

D. J. Bauer

MCCRUMB, F. R., Jr. **Recent Advances in the Study of Measles Virus.** [Editorial.] *Ann. Intern. Med.* 1959, Feb., v. 50, No. 2, 522–6. [17 refs.]

DAVOLI, R. & BARTOLOMEI-CORSI, O. **Researches on the Epidemiology and Viruses of Influenza in Florence (1941–1958).** *Scientia Med. Italica.* 1959, Jan.–Mar., v. 7, No. 3, 525–38. [26 refs.]

HEATH, R. B. & TYRRELL, D. A. J. **The Behaviour of some Influenza Viruses in Tissue Cultures of Kidney Cells of Various Species.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 8, No. 5, 577–91, 5 figs. [25 refs.]

The susceptibility of a variety of animal tissues to type A influenza and to Sendai viruses was studied by tissue culture methods. WS, swine and Sendai viruses were shown to multiply in cultures of kidney tissue from man, monkey, beef embryo, guineapig, rabbit, hamster, mouse and chick embryo. Virus multiplication was often accompanied by cytopathic effect which was particularly marked with Sendai virus. Serial propagation in monkey kidney cells was readily achieved with mouse-adapted virus strains (WS, NWS, PR8) but not with egg-adapted strains (A/England 1951, A/England 1954 and A/England 1956). Passage of WS and PR8 strains in monkey kidney cultures gave fluids with low infectivity to haemagglutination ratios. The virulence of PR8 for mice was increased after 10 serial passages in monkey kidney cultures but no similar change was observed with the WS strain. Tissue culture passage also resulted in loss of sensitivity of WS but not of PR8 to beta-inhibitor.

H. G. Pereira

HANNOUN, C. Effet de l'instillation conjonctivale de virus grippal chez le lapin et chez la souris. [**Effect of Conjunctival Instillation of Influenza Virus in Rabbits and Mice**] *Ann. Inst. Pasteur.* 1959, Feb., v. 96, No. 2, 170–77, 1 fig. [11 refs.]

Rabbits inoculated with live influenza virus (PR8) by the conjunctival route showed marked and persistent rises in homologous haemagglutination-inhibiting antibodies. The virus dose causing this effect was considerably smaller than that required to stimulate comparable antibody rises when given parenterally. Lower antibody rises were observed in rabbits receiving repeated conjunctival instillations of inactivated virus. Evidence suggesting that the immune response may be due to inapparent infection is presented and discussed.

The same virus strain administered to mice by the conjunctival route causes a number of fatal infections and no antibody rises in the surviving animals.

The possible use of the conjunctival route for the administration of attenuated virus vaccines is suggested.

H. G. Pereira

SOVINOVÁ, O. & LUDVÍK, J. **Electron Microscopic Study of the Influenza Virus** *A-equi-Praha/56. Acta Virologica.* Prague. 1959, Jan., v. 3, No. 1, 59–60, 3 text figs. & 3 figs. on 3 pls.

A virus isolated from horses with respiratory disease was studied by electron microscopy. The method of DAWSON and ELFORD [this *Bulletin*, 1949, v. 24, 1012], consisting of virus adsorption on to lysed erythrocytes, was employed. Purified virus preparations contained

spherical particles with a diameter of 50–150 mμ and filaments 80 mμ wide and 200–3,500 mμ long.

These results are in agreement with previous findings (Sovinová *et al.*, *Acta Virologica*, 1958, v. 2, 52), suggesting that the agent under study belongs to the type A influenza virus group. *H. G. Pereira*

Hollós, I. & Barna, A. **Electronmicroscopic Examination of Complete and Incomplete Influenza Viruses. II. Studies of the Fine Structure of Complete Influenza Virus.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 4, 389–97, 9 figs. [29 refs.]

The structure of influenza virus particles was studied by electron microscopy of ultra-thin sections of pellets of purified virus material obtained by centrifugation. A highly imaginative representation of the hypothetical structure of a virus particle is presented.

H. G. Pereira

Youngner, J. S. & Noll, H. **Virus-Lipid Interactions. I. Concentration and Purification of Viruses by Adsorption to a Cholesterol Column and Studies of the Biological Properties of Lipid-Adsorbed Virus.** *Virology.* New York. 1958, Aug., v. 6, No. 1, 157–80, 3 figs. [24 refs.]

The PR8 strain of influenza virus in the form of infected allantoic fluid was adsorbed to the extent of 87–100% when passed through a chromatographic column of ground crystalline cholesterol. After removal of cholesterol with ether 38% of the initial amount of haemagglutinin could be recovered from the column, the loss probably being due to inactivation by ether, and there was some indication of a concentration gradient of virus in different parts of the column. Adsorption still occurred when partially purified virus was resuspended in deionized water, and therefore did not require the presence of ions.

The kinetics of the adsorption process were investigated. Adsorption still occurred after the virus had been inactivated with formaldehyde. Analysis of the effluent showed that 93% of the protein impurities in the initial material were not retained by the column, thus giving a 15-fold increase in specific virus activity.

T_1 and T_2 phages, vaccinia and Newcastle disease viruses were also adsorbed by the column, but no adsorption occurred with the Parker strain of poliomyelitis virus. After resuspension of the cholesterol and inoculation of serial dilutions into chick embryos 21% of the adsorbed influenza virus could be recovered, and in similar experiments with vaccinia virus determined by plaque counting all the infective activity could be recovered from the column. Influenza virus adsorbed on to cholesterol gave an immune response after inoculation into chicks, and was still able to react with specific antiserum. *D. J. Bauer*

Borecký L., with the technical assistance of L. Maasová & J. Kianicková. **A Factor destroying Virus Receptors in Pneumococcal Cultures. III. The Effect of Pneumococcal Factor 103 (Pn-f-103) in Experiments *in vivo*.** *Acta Virologica.* Prague. 1959, Jan., v. 3, No. 1, 9–16, 1 fig. [14 refs.]

A pneumococcal factor destroying cell receptors for influenza viruses [Borecký, this *Bulletin*, 1959, v. 34, 292] was tested for its action on virus-cell interactions *in vivo*. Administration of the pneumococcal factor into the blood stream of guineapigs caused a gradual and temporary loss of red cell receptors for influenza viruses. The growth cycle of influenza viruses in deembryonated eggs treated with the pneumococcal factor before virus inoculation showed a prolonged eclipse phase. When administered to eggs after the virus inoculum, the factor limited virus multiplication to a single cycle. The pneumococcal factor affected haemagglutinin titres more markedly than infective titres. The factor was also shown to protect mice against infection by myxoviruses and this protection was particularly noticeable against Newcastle disease virus.

H. G. Pereira

Kundin, W. D., Robbins, Mary L. & Smith, P. K. **Inhibition of Influenza Virus Multiplication in Tissue Culture by Structural Analogs of Amino Acids.** *Virology.* New York. 1959, Jan., v. 7, No. 1, 1–27, 7 figs. [23 refs.]

The effect of amino acid analogues on the multiplication of influenza virus was studied with chick embryo lung tissue maintained *in vitro* as host system. Several methionine analogues (DL-norleucine, DL-ethionine, methionine sulphoximine, methoximine, acetyl-DL-ethionine and glycylnorleucine) inhibited virus multiplication and the inhibiting activity of all but methionine sulphoximine was reversed by DL-methionine, acetyl-DL-methionine, glycyl-DL-methionine, N-(4-chlorophenoxy-acetyl)-L-methionine but not by D-methionine. Virus multiplication was also inhibited by phenylserine and its ethyl ester, this action being reversed by phenylalanine and a number of its derivatives. Canavanine and canavanine flavianate exerted inhibitory action, reversed by L-arginine but not by D-arginine, proline, hydroxyproline, glutamic acid, citrulline, ornithine and histidine. The inhibitory action of canavanine flavianate appeared to result from a combination of the inhibiting activity of canavanine and a virucidal action of flavianic acid. Inhibition of virus multiplication by allylglycine and S-ethylcysteine was reversed by cysteine and cystine. The inhibitory action of S-ethylcysteine but not that of allylglycine was also reversed by homocysteine, cystathionine, glutathione and methionine.

Quantitative aspects of reversal of the inhibitory action of analogues are presented suggesting in several cases antagonism of a competitive nature. Reversal of virus inhibition was often accompanied by a parallel reversal of tissue toxicity.

Several analogues were found without effect on virus adsorption onto red cells and on the course of infection in fertile eggs and in mice.

A long list of amino acid and derivatives ineffective or partially effective against influenza A virus in chick embryo lung tissue cultures is appended to the paper.

H. G. Pereira

COHEN, A. & BELYAVIN, G. **Hemagglutination Inhibition of Asian Influenza Viruses: a New Pattern of Response.** *Virology.* New York. 1959, Jan., v. 7, No. 1, 59–74, 3 figs. [26 refs.]

The sensitivity of Asian influenza viruses to non-specific haemagglutination inhibitors was compared with that of formerly prevalent type A, A-prime and B strains. Asian strains varied in sensitivity to inhibitors. Sensitive strains reacted relatively poorly with egg-white α-inhibitor and with bovine serum β-inhibitor but were highly sensitive to inhibitors present in rabbit and in horse sera. It is suggested that at least 2 components are responsible for the inhibition of Asian strains by normal rabbit sera. One of these components is closely related, if not identical, with the α-inhibitor and the other is resistant to receptor-destroying enzyme (RDE). A new type of inhibitor was demonstrated in normal horse sera. This highly active inhibitor could be destroyed by trypsin but not by RDE and was partly removed from the sera by absorption with heterotypic virus strains. A correlation between haemagglutination-inhibition and virus neutralization was demonstrated with several serum-virus systems. The possible role played by non-specific serum inhibitors in natural infections is discussed with basis on the changing patterns of sensitivity to non-specific inhibitors shown by influenza virus strains isolated between 1934 and 1957. *H. G. Pereira*

BOGOCH, S., LYNCH, Patricia & LEVINE, A. S. **Influence of Brain Ganglioside upon the Neurotoxic Effect of Influenza Virus in Mouse Brain.** *Virology.* New York. 1959, Feb., v. 7, No. 2, 161–9, 2 figs. [11 refs.]

A purified brain ganglioside active as haemagglutination-inhibitor of influenza viruses was shown to inhibit the neurotoxic action of PR8 and NWS influenza virus strains for mice and the production of virus haemagglutinin in tissue cultures of chick embryo chorio-allantoic membrane. The anti-neurotoxic activity of the ganglioside could be demonstrated when this inhibitor was administered to mice before or at the same time as either of the 2 virus strains. Some inhibitory activity against the neurotoxic action of strain NWS was also observed when the ganglioside was administered to mice 2 hours after the virus inoculum. Anti-neurotoxic and haemagglutination-inhibiting actions of the ganglioside were comparable.

It is suggested that anti-neurotoxic action of the ganglioside may be due to competition with brain cell receptors for infecting virus. *H. G. Pereira*

ZHDANOV, V. M., HAMBURG, V. P. & SVET-MOLDAVSKY, G. J. **Antigenicity of the Inhibitor of Influenza Virus Strain A/Asia/57.** *J. Immunology.* 1959, Jan., v. 82, No. 1, 9–11.

Hens immunized against normal horse serum were shown to develop an antibody capable of neutralizing the heat-stable horse serum haemagglutination inhibitor active against Asian influenza virus. The anti-inhibitory activity of the antisera was observed with serum dilutions which were by themselves inhibitory, suggesting that the chicken serum inhibitor takes part in the reaction between antibody and horse serum inhibitor. No correlation was found between anti-inhibitory and precipitating antibodies present in the antisera.

H. G. Pereira

SOBIS, Halina & SZADOWSKA, Anna. Wpływ penicyliny, streptomycyny i sulfaitazolu na zmiany w płucach myszy zakażonych wirusem grypy. [**The Influence of Penicillin, Streptomycin and Sulphathiazole on the Changes in the Lungs of Mice infected by Influenza Virus**] *Med. Dośw. i Mikrob.* Warsaw. 1958, v. 10, No. 3, 357–66, 8 figs. on 4 pls. [27 refs.]

Mice infected intranasally with the PR8 strain of influenza virus were treated with penicillin, sulphathiazole and streptomycin. The subsequent mortality from pneumonia was higher than in an untreated control group (19–25 of 27, compared with 12 of 27), and death occurred earlier. The histological appearances in the lungs are described. The authors postulate that the earlier death in the treated mice is due to suppression of the bacterial flora which may favour the multiplication of virus. *D. J. Bauer*

KROEGER, A. V. & KEMPF, J. E. **Inactivation of the Influenza Virus by Low Voltage Roentgen Rays.** *J. Bacteriology.* 1959, Feb., v. 77, No. 2, 237–46, 5 figs. [24 refs.]

Inactivation of the infective and haemagglutinating properties of influenza virus (strain PR8) by X-rays was investigated and several factors influencing inactivation curves are presented. Inactivation of virus infectivity followed an exponential curve with a 37% survival dose of $6{\cdot}5 \times 10^4$ r from which a target diameter of 42 mμ was estimated. Inactivation of the haemagglutinating activity was affected by the method of drying the virus, the protective materials used in drying and the method used for virus purification. For virus preparations concentrated by ultra-centrifugation, the haemagglutinin inactivation curve was not exponential, with increasing sensitivity for the larger X-ray doses. The haemagglutinin of virus materials concentrated by red-cell adsorption and elution gave nearly linear survival curves with a 37% survival dose of $6{\cdot}2 \times 10^5$ r and an estimated target diameter of 17 mμ. Similar preparations treated by ether gave linear haemagglutinin-inactivation curves with a target diameter estimated to be 23 mμ. It is suggested that the higher sensitivity of ether-treated haemagglutinin may be due to loss of virus protein by denaturation.

H. G. Pereira

BLASKOVIC, D., RATHOVÁ, V. & BORECKÝ, L. **Antigenic Relationships to Myxoviruses of a Virus isolated from a Respiratory Infection in Ducks.** *Acta Virologica.* Prague. 1959, Jan., v. 3, No. 1, 17–24. [16 refs.]

A virus isolated from ducks was compared with agents of the myxovirus group by serological and haemagglutination tests. Complement-fixation tests revealed

a close relationship between the duck virus and influenza A, mumps and Newcastle disease viruses. The duck virus was clearly distinguishable from other agents of the myxovirus group by haemagglutination-inhibition and serum neutralization tests. Results are presented suggesting that haemagglutination-inhibiting antibodies for the duck virus are thermolabile. The duck virus was found to possess a marked capacity to react with and destroy cell receptors.

It is suggested that the duck virus is a new myxovirus belonging to the type A influenza group.

H. G. Pereira

LIEBERMAN, M. & FRIEDMAN, M., with the technical assistance of C. KASPER. **Growth Characteristics of Adenoviruses. I. Production and Release of Complement Fixing Antigen and Infectious Virus.** *J. Immunology.* 1959, Jan., v. 82, No. 1, 1–8, 4 figs. [24 refs.]

Growth curves of adenovirus types 1, 4, 5 and 6 in HeLa cell cultures were studied with a view to the possible correlations between production and liberation of infective virus and complement-fixing antigen and development of cytopathic effect. The 4 virus types under study showed similar growth characteristics. HeLa cell cultures inoculated with 0·1 ml. of undiluted virus materials containing $10^{2\cdot5}$ to $10^{4\cdot5}$ 50% infective doses (based on titrations read at 7 days) showed initial production of intracellular infective virus and complement-fixing antigen at 16 to 22 hours. Release of virus and complement-fixing antigen from the cellular phase was slow and incomplete. Cytopathic effect was found sometimes to precede the onset of virus multiplication.

It is suggested that the complement-fixing antigen is not a precursor to infective virus but represents a by-product of the infectious process. *H. G. Pereira*

NÁSZ, I. & TÓTH, M. **Studies on the Cytopathic Changes caused by Different Types of the Adenovirus Group in Human Amnion and Detroit-6 Cell Cultures.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 4, 377–82, 10 figs. [14 refs.]

Adenovirus types 3, 4 and 7 could be distinguished from types 1, 2, 5 and 6 by the characteristics of cytopathic effects in cultures of human amnion cells but not in the Detroit-6 cell line. The main distinguishing feature of the cytopathic effect caused by types 3, 4 and 7 consisted of the formation of a network of rounded cells which is contrasted with loosening and a more complete cellular degeneration caused by types 1, 2, 5 and 7.

[See also BARSKI, this *Bulletin*, 1957, v. 32, 290; BOYER *et al.*, *ibid.*, 1957, v. 32, 818.] *H. G. Pereira*

GINSBERG, H. S. & DIXON, Mary K. **Deoxyribonucleic Acid (DNA) and Protein Alterations in HeLa Cells infected with Type 4 Adenovirus.** *J. Exper. Med.* 1959, Apr. 1, v. 109, No. 4, 407–22, 3 figs. [28 refs.]

BALUDA, M. A. **Loss of Viral Receptors in Homologous Interference by Ultraviolet-Irradiated Newcastle Disease Virus.** *Virology.* New York. 1959, Mar., v. 7, No. 3, 315–27, 2 figs.

CHURCHER, Gilliam M., SHEFFIELD, F. W. & SMITH, W. **Poliomyelitis Virus Flocculation: the Reactivity of Unconcentrated Cell-Culture Fluids.** *Brit. J. Exper. Path.* 1959, Feb., v. 40, No. 1, 87–95.

The authors have previously described a flocculation reaction between polioviruses and specific antisera [this *Bulletin*, 1956, v. 31, 958, 1172]. A major difficulty with this technique has been the necessity to concentrate the virus obtained from infected tissue cultures before sufficiently strong antigens were obtained. They have now found that higher titre antigens can be obtained from infected cultures of ERK cells which will react in the flocculation test without any further concentration. The best virus flocculating antigen was obtained by a 2-stage method. In the first stage virus was harvested from a normal monolayer culture of ERK cells and was then held in a lightly plugged vessel at room temperature for several days to allow the escape of CO_2. 4·4 ml. of this virus fluid plus 2·5 ml. of normal rabbit serum and 0·1 ml. of 5% glucose were then added to a baby's feeding bottle in which a sheet of cells had been grown on all 6 glass surfaces. This was achieved by seeding each bottle with about 40×10^6 cells suspended in 50 ml. of medium and rotating it on a roller machine at 36°C. After 2 days the nutrient fluid was removed and replaced by the virus inoculum. This method was equally successful for virulent and attenuated polioviruses but slight differences were made in the constitution of the medium for attenuated viruses. With this method infectivity titres of $10^{8\cdot9}$, 10^8 and $10^{8\cdot7}$ per ml. were achieved for the Brunhilde Type 1, Y-SK, Type 2 and Leon Type 3 strains of virus. The antigens prepared in this way from both virulent and attenuated strains proved to be good flocculating antigens and they were superior to virus prepared from suspended cell cultures. A Type 1 poliovirus antigen was treated for various periods at 4°C. with 1/4,000 and 1/2,000 formalin. It still retained its power to flocculate with specific immune serum unimpaired up to at least 107 days in formalin. Some sera obtained after prolonged immunization of rabbits gave cross reactions between the 3 types of poliovirus in the flocculation reaction. These cross reactions were shown to be due to antigens to ERK cells since they could be adsorbed with ERK cells. ERK cells were originally employed because it was hoped that their rabbit origin would preclude the appearance of antibodies to ERK cells in rabbits immunized with virus grown on these cells but this hope was vain. The authors contend that the very high titres of poliovirus that can be obtained from ERK cells is a cogent argument for the adoption of these cells for poliovirus vaccine production "if and when the hypothetical risks associated with potential malignancy are judged to be negligible". *A. J. Beale*

SALZMAN, N. P. & LOCKART, R. Z., Jr. **Alteration in Ribonucleic Acid Metabolism resulting from Poliomyelitis Virus Infection of HeLa Cells.** *Biochim. et Biophys. Acta.* 1959, Apr., v. 32, No. 2, 572–3.

WARREN, J., HARE, J. D. & GOLDMAN, Cynthia. **Complement-Fixing Antigens of Living and Inactivated Poliovirus. II. Complement-Fixing Activity of Poliomyelitis Vaccine and its relation to Immunogenic Potency.** *Amer. J. Pub. Health.* 1959, Jan., v. 49, No. 1, 53–61, 5 figs. [10 refs.]

Potency tests on poliovaccine are not very satisfactory and the authors have investigated the complement-fixing (CF) antigen content as a measure of vaccine potency. The sera were prepared by inoculating guineapigs with the fluid from infected HeLa cells. Normal commercially prepared vaccine had to be concentrated 30–100-fold before it would react in complement-fixation tests. Material from 2 manufacturers was tested at intervals during inactivation and although the amount of CF antigen varied widely there was about a 2-fold fall in titre between the start and the end of inactivation. The CF antigen measured was not directly related to antigenic potency since vaccine concentrated by dialysis and freeze-drying retained its CF antigen while the antigenicity was almost completely destroyed. The authors none the less believe the method has application to the control of poliovaccine manufacture.

[Most poliovirus preparations contain at least 2 complement-fixing antigens usually called D and C. Similarly most sera contain both antibodies. The D antigen content only is probably related to antigenic potency of poliovaccine. Therefore, in using the CF test to estimate poliovaccine potency a test only detecting D antigen is required.] *A. J. Beale*

FARRELL, Leone N. & REID, D. B. W. **Disc-Plate Assay of Poliomyelitis Antibodies.** *Canadian J. Pub. Health.* 1959, Jan., v. 50, No. 1, 20–26, 1 fig. [21 refs.]

A method of titrating poliovirus antibodies is described in detail. This depends upon measuring the zone of inhibition of poliovirus action produced by serum soaked on to a filter paper disk. The disk is placed on to an agar overlay on monkey kidney cells infected with poliovirus. It was found that there is a linear relationship between the diameter of the zone of inhibition and the logarithmic dilution of the antiserum. The strength of one serum in terms of another standard serum can be determined from 2 dilutions of each on a single plate with a standard error of about 14%. The method was used successfully for titrating poliovirus antibodies in sera of monkeys, rabbits and chicks. The method was found to give comparable results to the metabolic inhibition test for the titration of the potency of poliomyelitis vaccine by means of the chick potency test recommended by the U.S. Division of Biological Standards.

[This appears to be a valuable method of antibody assay and the paper gives full details.] *A. J. Beale*

LENKEVICH, M. M. & IL'ENKO, V. I. **The Experimental Chemotherapy of certain Virus Infections.** *Problems of Virology.* London. 1958, v. 3, No. 1, 52–4, 1 fig. [Translated from Russian.]

This paper from Leningrad briefly records some success in the treatment of experimental neurotropic virus infections with organic phosphorus compounds which are cholinesterase inhibitors. Mice were inoculated intracerebrally with Type 2 poliomyelitis virus (Lansing strain): all controls died, but a recovery rate of 40%, and longer survival in animals dying, was obtained by treatment with phosarbin (tetraethylmonothiopyrophosphate), together with diphacil (described as a "complex ether of diethylaminoethanol and phenylglycollic acid"): this substance is said to have been used "as an antidote". Titrations of virus in the brain showed a similar content up to the 5th day, when it fell in treated animals and increased in controls. In some experiments barbiturates were given with phosarbin, with what is considered to have been promising results. Some effects were also observed on influenza virus infection in mice and on infection with Taylor's encephalomyelitis virus in guineapigs.

L. P. Garrod

HOTCHIN, J. E. & CINITS, M. **Lymphocytic Choriomeningitis Infection of Mice as a Model for the Study of Latent Virus Infection.** *Canadian J. Microbiol.* Ottawa. 1958, Apr., v. 4, No. 2, 149–63, 1 fig. [38 refs.]

A study has been made of latent infection of mice with the WE strain of lymphocytic choriomeningitis virus. In preliminary experiments it was found that exposure of adult mice to X-rays or treatment with cortisone would confer a considerable degree of protection against subsequent intracerebral infection with the virus. The survival time and percentage mortality after intracerebral infection was studied in mice of various ages; mice aged up to 3 days showed prolonged survival (15–20 days) and a mortality of around 20%, but after 4–6 days of life the survival time fell to 10 days and the mortality began to rise, attaining 100% in mice aged 5–10 weeks. Mice infected on the 1st day of life showed no signs of illness, but infective virus in high titre was found in the brains for as long as 6 months. No signs of infection could be produced in the mice by intracerebral injections of starch and similar materials, or by exposure to cold or X-rays. The animals were immune to intracerebral infection with western equine encephalomyelitis virus but were not immune to ectromelia. The results show that lymphocytic choriomeningitis virus is only pathogenic for mice if they are able to develop an immune response to it as a foreign antigen, and the resemblance to immunological tolerance to skin homografts is pointed out. The type of latent infection produced is distinct from inapparent infection, which can be reactivated by challenge procedures, and the authors propose the term "vital infection" to describe it. *D. J. Bauer*

DOHERTY, R. L. **Effects of Yellow Fever (17D) and West Nile Viruses on the Reactions of Human Appendix and Conjunctiva Cells to Several other Viruses.** *Virology.* New York. 1958, Dec., v. 6, No. 3, 575–83. [16 refs.]

Conjunctiva cells infected with 17D virus continued to support virus multiplication for at least 21 days

without detectable cytopathic effect. In appendix cells 17D caused cytopathic effects after 5–8 days but not all cells were affected and the survivors regenerated a sheet of cells which then continued to support virus multiplication without cytopathic effect. Similar results were obtained with a strain of West Nile virus isolated from a human patient in Israel. A neutralization test could be performed, the cytopathic effect described being used, but immune serum did not affect virus multiplication in the stable infected cell lines. Starvation of the cultures by omission of horse serum from the medium did not affect virus production in the cultures of stable infected lines which recovered. The relative susceptibility of mice and appendix cells to 17D virus varied with the source of the virus. Appendix cells infected with 17D and West Nile viruses were unaffected by superinfection with 17D or West Nile viruses, while polioviruses and herpes virus caused degeneration of the cultures which was delayed and of lower titre compared with that in uninfected appendix cells. Conjunctiva cells infected with 17D resisted West Nile but not polioviruses or herpes. All 3 infected cell lines were fully susceptible to vaccinia virus. West Nile virus caused fatal infections in mice by the intraperitoneal route while 17D virus did not. This was used to show that appendix cells infected with 17D could be infected by 100 LD50 or more of West Nile virus without cytopathic effect.

2 hypotheses are advanced to account for the findings: (1) they are evidence of interference, or (2) the initial cytopathic effect in appendix cells selects a cell population capable of supporting virus multiplication without cytopathic effect. The latter gains some support from the absence of resistance to polioviruses and herpes in infected conjunctiva cells where the initial cytopathic effect does not occur.

C. E. Gordon Smith

SHUBLADZE, A. K. **On Some Viruses related to the Etiological Agent of the Spring-Summer Tick-Borne Encephalitis.** *Acta Virologica.* Prague. 1958, Oct.–Dec., v. 2, No. 4, 255–9, 1 fig. [21 refs.]

This is a useful summary of the history, epidemiology and clinical features of infections with a number of viruses related to Russian spring-summer encephalitis virus which have been isolated in recent years by workers in Russia and Eastern Europe. It should be read in full. The viruses discussed are (1) the "mouse-paralysing virus" which was isolated from *Mus musculus* and is known to have caused one human case. (2) The Conan encephalitis virus isolated in a small human outbreak of unusual central nervous system disease with 7 deaths in 10 cases. (3) The virus of Omsk haemorrhagic fever. (4) The biphasic encephalomyelitis virus. (5) The virus of "encephalitis with amentive syndrome" which was isolated very late in the course of a central nervous system disease. (6) "Latent rat virus" isolated from a house rat. The host pathogenicity of these viruses is tabulated for laboratory animals. They are stated to be serologically identical. [This is a summary only and some of these "new" viruses and their origin must be accepted with caution.]

C. E. Gordon Smith

GAIDAMOVICH, S. I. **Study of a Virus isolated from an Encephalitis Patient with Amentia Syndrome.** *Problems of Virology.* London. 1958, v. 3, No. 3, 160–66. [Translated from Russian.]

A stoker aged 24 years had fever and severe headache lasting several days. 8 days after onset, although still unwell, he returned to work. 5 days later he developed mental confusion and insomnia for which he was admitted to hospital. He was afebrile with marked mental confusion, marked abnormalities in his reflexes, some spasticity, but no evidence of meningism. 4 months after the original onset he still showed no improvement so blood and cerebrospinal fluid were taken for virus isolation. A slow recovery began about a month after this and a month later he was discharged from hospital normal except for minimal reflex abnormalities.

A virus was isolated from the blood in mice at the first passage: 3 of 8 mice died 7, 9 and 14 days after inoculation and another was paralysed on day 7. The virus was filterable and pathogenic for mice by all routes. The incubation period intracerebrally was 4–5 days and the titre reached in the brain 10^{-6} to 10^{-7}.

Two-thirds of the guineapigs inoculated became febrile 3–7 days after inoculation and died on days 10–13. All lost 10–25% of body weight. Virus was isolated from the febrile but not the dead guineapigs. Some newborn guineapigs inoculated became paralysed. About half the rabbits inoculated became febrile but recovered and developed antibodies. Suckling but not adult cotton rats were irregularly affected and white rats, kittens and chicks were insusceptible.

Histology of the brains of affected animals showed swelling of vascular endothelium, perivascular cuffing, diffuse infiltration of the grey matter, and marked neuronal destruction. The lateral ventricles were dilated and the choroid plexus oedematous and variably infiltrated.

Virus could be isolated by various routes of inoculation in the chick embryo in which the highest titre of virus was in the brain.

The patient's serum had complement-fixing antibody to a titre of 1 in 20 on the 54th and 125th days of the disease. Neutralizing antibody was absent on the 14th, 34th and 54th days but the neutralizing index was 47 on the 125th day.

Comparison by neutralization tests showed that the virus was closely related to those of Russian spring-summer encephalitis and Konansk encephalitis [apparently of same group]. No relation was found to "acute human encephalomyelitis", lymphocytic choriomeningitis, herpes, western and eastern equine encephalomyelitis, and encephalomyocarditis viruses. The virus was "closely related to the paralytic virus of domestic mice and the latent virus isolated from rats".

[This latter piece of information and the low titres of antibody found in the patient, together with the remarkably late stage of the disease at which virus

was apparently isolated, prompts the question of whether this may not have been a virus picked up from the mice.] *C. E. Gordon Smith*

PANTHIER, R., BRES, P., HUSSON, R. A. & HANNOUN, C. Étude des anticorps sériques provoqués par la vaccination antiamarile. [**Study of the Serum Antibodies evoked by Yellow Fever Vaccination**] *Bull. Soc. Path. Exot.* 1958, July–Aug., v. 51, No. 4, 589–600.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 713.]

IMMUNITY

MIR CHAMSY, H., SOHRAB, V. & KROUR, A. Établissement de l'immunité et élaboration des anticorps neutralisants et agglutinants, chez le lapin, par injection de virus de la vaccine incorporé dans les vaccines associés. Rôle des injections de rappel. [**Immunization and Formation of Neutralizing and Agglutinating Antibodies in Rabbits after Injection of Vaccine Virus incorporated in Combined Vaccines; Role of Booster Doses**] *Rev. d'Immunologie.* 1958, Oct.-Dec., v. 22, Nos. 5–6, 553–66, 5 figs. [33 refs.]

The authors tested in rabbits the efficacy of a tetravalent vaccine consisting of diphtheria and tetanus toxoids, killed *Bordetella pertussis* and chick-embryo-adapted vaccinia virus elementary bodies. The vaccinia virus ($7{\cdot}5$–10×10^4 infectious units per dose) was adsorbed on aluminium phosphate with the other antigens. Sera were examined by paper electrophoresis and tested for diphtheria and tetanus antitoxins and for vaccinal neutralizing and agglutinating antibodies. Antibodies to *B. pertussis* were disregarded. Resistance to vaccinia virus was tested by challenging the immunized animals with a potent lymph. 3 injections of tetravalent vaccine at intervals of 20 days were followed by steadily increasing serum antitoxin levels, vaccinial neutralizing indices and vaccinial agglutination titres. 20 rabbits were given a diphtheria-vaccinia vaccine prepared 9 months previously and stored at 4°C. When challenged with a potent lymph, 2 rabbits developed a few discrete pocks while 18 were completely protected.

The authors recommend that vaccinia virus should be added to the triple antigen commonly used to immunize children. [It would, however, be wiser to await the results of further work before adopting the suggestion.] *Colin Kaplan*

DIACONO, H. & CASTAY, Mathilde. Détermination de la properdine humaine par utilisation de sérum de cobaye antiglobules rouges humains. [**Determination of Human Properdin by the Use of Guinea-pig Antiserum Prepared Against Human Red Cells**] *C.R. Soc. Biol.* 1958, v. 152, No. 10, 1346–9.

MIYA, F., MARCUS, S. & THORPE, B. D. **Effect of Properdin on Whole Body Irradiated Mice and Rats.** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 757–61, 2 figs. [13 refs.]

The mortality rates in groups of mice exposed to 550r total body irradiation were not changed by the intravenous injection of 50 units of partially purified properdin on the 1st, 3rd, 5th or 7th day after irradiation. Death was delayed in the group which was given properdin on the 1st day and accelerated in the group treated on the 7th day. In a similar experiment with purified human properdin no protection at all was given. Neither large intraperitoneal doses of properdin nor the administration of guineapig complement as well as properdin gave any protection to the animals. Similar results were obtained when rats were used instead of mice. *Sheila McDonald*

KORÍNEK, J. & PALUSKA, E. Technika isolace skupin antigenů lidského séra elektroforetickou frakcionací, umožnující srovnání antigenní příbuznosti proteinů metodou precipitace v agarovém gelu. [**A Technique for the Isolation of Antigen Groups of Human Serum by Electrophoretic Fractionation, providing the Possibility of comparing Antigenic Relationship of Proteins by the Method of Precipitation in Agar Gel**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1958, v. 7, No. 5, 289–97, 5 figs. (3 on 2 pls.) [36 refs.] English summary.

The authors have developed a method of electrophoretic separation of serum proteins which can be combined with subsequent investigation of the fractions by the gel diffusion technique. A glass plate 18 × 5 cm. is covered with an even layer of 22·5 cc. of 1% agar in *p*H 8·5 veronal buffer of ionic strength 0·05. A starting well of 3 × 1 cm. is cut out near one end and filled with a mixture of buffered agar and the serum to be investigated. Electrophoresis is then carried out in the usual way for 4–5 hours with a potential difference of 3·2 volts per cm. The position of the fractions is then determined by taking an impression of the surface of the agar on Whatman No. 1 paper and staining it with bromophenol blue. The stained paper is then placed under the glass plate and disks containing the fractions are cut out with a cork borer; the disks are then transferred to the peripheral wells of an Ouchterlony plate containing antiserum in the centre well, and antigenic analysis by diffusion precipitation is then carried out in the usual way. *D. J. Bauer*

Miscellaneous

BEECHER, H. K. **Experimentation in Man.** [Report to the Council on Drugs (KAUTZ, H. D., Secretary) adopted by the Committee on Research (DE NOSAQUO, N., Secretary).] *J. Amer. Med. Ass.* 1959, Jan. 31, v. 169, No. 5, 461–78. [Numerous refs.]

Although in most cases the problems of human experimentation do not lend themselves to rigid rules, one purpose of this study is to set down the views, concepts and even "rules" that have been accepted by one group or another so that an investigator, troubled by a problem, can find reference to past thinking and measure his problem in terms of the experiences of others. Prior experimentation in animals is essential, whenever possible, but the crucial study of new techniques and therapeutic agents must necessarily be carried out in man. The rapid increase in therapeutic measures in recent years has thrown a heavy load on the experimentalist and as a result man as the final test site has increasingly come into prominence. It is often not possible to transfer observations made in normal individuals to the sick and the latter must therefore be taken as subjects. To obtain the consent of the patient is not in itself enough since the considerations involved are often so technical that they cannot be made clear to the layman and, in the doctor/patient relationship, he is likely to agree to any proposal made.

The responsibilities on those who undertake experimentation in man are so great that whenever even remote hazard is a possibility, group decision supported by a proper consultative body should be employed. Any classification of human experimentation as "for the good of society" is to be viewed with distaste and even alarm. General rules may well do more harm than good. For example, a rigid interpretation of the Nuremberg Rule 1 (the voluntary consent of the human subject is absolutely essential) would cast considerable doubt not only on the propriety of studying mental disease but also on the use of placebos. Detailed explanation to the participating subjects would nullify the value of placebos and yet they are occasionally needed for the guidance of the able, responsible physician as well as the treatment of the patient.

[These are some of the reflections in a thoughtful, though somewhat repetitive, article that cannot be adequately summarized and should be read in the original.] *A. Bradford Hill*

Book Reviews

HUNTER, Donald. **Health in Industry.** 288 pp., 18 pls. Pelican Med. Ser. A441. Harmondsworth: Penguin Books Ltd., Middx. [4s.]

This is written by an eminent hospital physician who describes some of the more interesting occupational diseases. More than half the space is devoted to a description of poisoning by various metals and organic compounds, dust diseases of the lungs and other occupational diseases such as cancers, dermatoses, radiation hazards and diseases due to infections. There are other chapters on the history of industrial medicine, accidents at work and legislation affecting the worker, a useful glossary of technical terms and suggestions for further reading. The latter is broad enough to suit almost anyone who may be interested in this subject.

This book will be particularly useful to medical students, doctors and nurses as an attractively written introduction to industrial medicine, with plenty of facts and clear descriptions of how the occupational diseases may be treated and prevented. It should also interest the many who are not in medicine but who have responsibilities for health in industry.

Occupational Health is such a broad subject that it would not be possible for one man to cover it adequately in one book of less than 300 pages. Sensibly, the author has restricted his chapters to subjects which interest him and so he is able to interest his readers.
R. S. F. Schilling

HARMSEN, Hans, with Karl-Heinz WEBER *et al.* Die Integration heimatloser Ausländer und nichtdeutscher Flüchtlinge in Westdeutschland. Ergebnisse einer sozialbiologischen Strukturanalyse der 1954/1955 noch in Lagern, Wohnheimen und Wohnsiedlungen sowie in Heimen und Krankenhäusern erfassten 53642 nichtdeutschen Flüchtlinge. 132 pp., 1 map. 1958. Augsburg: Hofmann-Druck, Kreitmayrstr. Germany. [DM 5.–.] [**Homeless Foreigners in the Federal Republic of Germany.**]

This book is the first volume to be published for the German Nansen Society which was founded in 1957. It contains the results of a socio-biological investigation and analysis of over 50,000 homeless foreigners who in 1954–5 still remained in camps, homes, hospitals and settlements in different parts of Western Germany.

The first part of the book gives an interesting historical outline, entitled "The irruption of the new barbarism", from the Balkan War of 1912 to the present day, of the extermination or displacement of peoples to serve the ends of national ideologies. This

is followed by a description with a number of numerical tables of the extent to which nationals became displaced persons or refugees during the Second World War, of the numbers who have now been repatriated and of those cared for by the International Refugee Organization and the United Nations Relief and Rehabilitation Administration.

The other 4 parts of the book set out the results of the special investigation of 53,642 remaining refugees who had not been absorbed in 1954–5. These deal with: (1) age and sex constitution, family composition, domestic circumstances, mental illness and tuberculosis, (2) the construction of the settlements, errors in their planning and social problems which have arisen, (3) problems in relation to employment and (4) a summary of the most important facts and problems with discussion of immediate needs for their amelioration.

This book is in handy form and its 132 pages of relatively small print contain an admirable wealth of detail, description and discussion which does credit to the industry and thought of the author and his group of co-workers. *M. E. Delafield*

BAKER, George [M.D., F.R.S.]. **An Essay concerning the Cause of the Endemial Colic of Devonshire, 1767.** 60 pp., frontpiece. Reprinted by the Delta Omega Soc., 1958. New York 19: Book Service, American Public Health Association, 1790, Broadway, N.Y. [$5.00.]

The public health world is under a deep debt of gratitude to the Delta Omega Society of America for another facsimile reproduction of a classic. This is the fourth and its predecessors have been William Budd's *Typhoid Fever, Snow on Cholera* and *Panum on Measles.*

Dr. HUNTINGTON WILLIAMS of Baltimore, a bibliophile well known on both sides of the Atlantic, is the editor and in the introduction quotes at some length from Simon's *English Sanitary Institutions.* The reprint is dedicated to another famous Baltimorean, Dr. William H. WELCH, a founder of the Johns Hopkins School of Public Health.

Sir George Baker, Bart., M.D., F.R.S., as he eventually became, was born in Devonshire in 1722. He settled in London in 1761 and died in 1809. He was elected President of the Royal College of Physicians of London in 1792 and again in 1795. The reprint contains a reproduction of the portrait of Sir George which hangs in the College. He was a busy physician and was physician to the Queen's Household.

The essay on the cause of the Devonshire colic was read at a meeting of the College on June 29, 1767 and printed the same year. It demonstrates the process by which he proved beyond reasonable doubt that Devonshire colic was, in fact, lead poisoning. Sir George dedicated his essay to the members of Parliament for the county no doubt in the hope that they would take steps "to remove the source of so much mischief".

There are many quotations from the writings of others and, as was the custom of the time, they are in Latin which in those days was the language used by educated people in every country, for the communication of advances in knowledge.

The early writers on Devonshire colic, Musgrave (1703) and Huxham (1739), thought that the illness was due to the acidity of cider but Baker could not reconcile that theory with the absence of the disease from cider drinkers in other counties, from sherbet drinkers in Turkey or jockeys who took vinegar to reduce their weight. Further the wines of Tubinga, though very acid, did not produce similar symptoms until they began to be adulterated with lithage.

Baker first ascertained the geographical distribution of the disease and discovered from Dr. Wall of Worcester that the only cases where, to his knowledge, the colic of Poitou had occurred was when a farmer had stored cider in a leaden cistern. Normally no lead was used in that district in the containers for cider at any stage but in Devonshire it was common practice to seal the joints in the vats and other containers with lead. Baker tested in Exeter samples of local cider and "Must", found lead in them and had his results confirmed by a chemist when he got back to London. The tests were qualitative as, at that time, quantitative analysis was unknown or in its infancy.

5 separate sets of experiments are described and they proved his hypothesis.

Medical disputation was as common then as now and several pages are devoted to refuting the arguments of "a certain Seerup, a physician of Copenhagen" who averred that there was no danger in adding lithage to wine.

Baker says "*Sine experientia vana omnis theoria*", and thus echoes the teaching of John Hunter and all medical investigators. *Allen Daley*

AINSWORTH, G. C. [Ph.D., F.L.S.] & AUSTWICK, P. K. C. [B.Sc., F.L.S.] **Fungal Diseases of Animals.** 148 pp., illustrated. 1959. Farnham Royal: Commonwealth Agricultural Bureaux, Central Sales Branch, Nr. Slough, Bucks. [20s.]

In the study of medical mycology it is impossible to ignore veterinary mycology, not only because of the role of animals in the transmission and spread of many of the mycoses, but also because the majority of the pathogenic fungi which affect man also affect animals. Indeed, the student of medical mycology has much to gain from a study of veterinary mycology, for, while the infective processes are much the same in both animal and man, material for pathological study is much more easily available from animals than from man. Moreover, for a variety of reasons, the natural history of mycotic disease can best be studied in animals.

Medical mycologists and pathologists as well as veterinarians are fortunate that two such eminent students of medical and veterinary mycology have collaborated in writing this important book. All the superficial and deep mycoses of animals which occur in Great Britain and elsewhere are described, largely from personal experience. Especially is this the case with the very full descriptions accorded to aspergillosis and moniliasis in animals; moreover, the text concerning

these important and widespread diseases is especially favoured by magnificent illustrations, not only in black and white, but also in colour. For the sake of completion, diseases with a more restricted geographical distribution, such as coccidioidomycosis, histoplasmosis and North American blastomycosis are included. The book is well planned, and the information clearly set out under separate headings which appear consistently throughout this book for most of the diseases described. The chapters on mould toxicoses and poisoning by larger fungi provide an unexpected and stimulating climax to this valuable treatise on animal mycopathology.

The text is clearly printed, by lithography, and the clinical and pathological features of the various diseases are amply illustrated. The binding is in blue cloth. The encyclopaedic contents compressed into this small volume are offered at the modest price of 20 shillings.

C. J. P. La Touche

COLTART, Margaret [M.A., A.M.I.A.], RAINE, Helen [B.A.] & HARRISON, Elizabeth. **Social Work in Tuberculosis.** 144 pp. 1959. London: The Chest & Heart Association, Tavistock House North, Tavistock Square, W.C.1. [12s. 6d.; $3.00.]

Though tuberculosis is by no means the scourge now that it was a few decades, or even years, ago it is foolish to regard it, as some do, as a disease to which little attention need be paid by public authorities. Its impact on domestic and economic life is still very serious and this excellent little book by social workers who are in daily contact with the problems indicates what is being done.

There are heart-rending illustrative case reports, and the tragic drama of chronic and infectious disease when it strikes a family is well brought out. There are glimpses, too, of the grave difficulties which arose at the time when the number of beds was totally inadequate.

It is demonstrated that the social aspect of the disease has many facets and that each patient presents an individual problem; there is no set pattern.

The first 7 chapters are written by the Head Almoner of the Brompton Hospital, London; the next 2 by the Tuberculosis Welfare Officer of the Middlesex County Council and the last by an officer of the Chest and Heart Association, formerly the National Association for the Prevention of Tuberculosis.

There are 3 chapters on Readjustment to Normal Life. The 2 special features of rehabilitation of the tuberculous are infectivity and risk of relapse. There are 15 Industrial Rehabilitation Units of the Ministry of Labour and National Service and in recent years 22% of those admitted have been tuberculous. There are 14 government training centres for Vocational Training and 4 voluntary residential colleges. Other rehabilitation institutions are 90 Remploy factories, of which 7 are for the tuberculous, which give employment to 700 tuberculous persons. There are 3 sanatorium units where university education can be continued and 5 village settlements. The pioneer, Papworth, now has 1,500 residents and some non-tuberculous subjects are admitted.

To adopt the phraseology of a recent book on general practice this book describes *good* social work in tuberculosis. It is possible, indeed probable, that this standard is not attained everywhere. There is no legal bar but the two main ingredients, money and a sufficiency of trained workers, are both in short supply. Nevertheless, the provision of a good social service for the alleviation of the lot of the tuberculous should have a high priority.

Allen Daley

UNITED STATES ARMY, MEDICAL DEPT. **Preventive Medicine in World War II** [COATES, John Boyd, Jr. (M.C.), Editor in Chief.] **Vol. IV. Communicable Diseases transmitted chiefly through Respiratory and Alimentary Tracts.** pp. xxi + 544, 48 charts. 1958. Wash. 25: U.S. Govt. Printing Office. [$5.50.]

The arrival of this long awaited publication will be of particular interest to those who specialize in the epidemiology of communicable disease. Although the scope of the book is wide, it will be of value only to a limited following today. It is indeed unfortunate that the statistical evidence has had to wait 13 years before it has become available.

This attempt to summarize the history of war experiences is no mean achievement; the book has been divided into 3 parts, the first of which, by Professor John E. GORDON, serves as an admirable introduction and summary. The rest of the volume is divided into a series of chapters, each of which follows the same pattern: beginning with the history of the disease as far as the United States Army has been concerned, it then gives an account of the military experience of World War II in the various theatres compared with that in the continent of North America; the clinical aspects and methods of prevention and control are given in logical sequence. Some of the sections approach the subject of failure too briefly and there are some unexpected omissions like that of infective hepatitis, which it is hoped will be described in later volumes.

Among the diseases spread through the respiratory tract, the chapter on influenza is of particular interest, while that on tuberculosis follows the experience of other armies using screening methods for recruits. The record of the intestinal infections was surprisingly good though, as expected, the dysenteries and especially amoebiasis were the common cause of sickness. In tropical countries fungus infections assumed importance and, in the United States, coccidioidomycosis became a special problem.

Complete in itself, this volume gives a clear picture of the way in which the military medical authorities met the challenge of these diseases. Its main value, however, is to provide a useful historical reference. The United States Army has every reason to be proud of its achievements.

W. R. M. Drew

SWIFT, Stewart [M.B.E.]. [Edited by] **Sanitary Officers Practice: Environmental Hygiene.** pp. xv + 781 + 58, numerous figs. 1958. London: Butterworth & Co. (Publishers) Ltd. [85s.]

This is the fifth and final volume in a series called *Sanitary Officers Practice.* It is in 10 parts, each

written by an author of much experience in his particular subject in especial relation to public health practice. This book, with its companion work on *Food Inspection* in this series, is intended to cover " the whole field of public health practice coming within the sphere of the public health inspector ". Legal and administrative matters are referred to briefly when they are essential to the practical aspects: they are dealt with in detail in the other 3 volumes of the series on sanitary, food and drugs and housing administration.

The subjects included in the 10 parts of the book are:—(i) air, ventilation, heating and lighting, (ii) water supply, (iii) environmental diseases, (iv) rodent and insect pests, (v) atmospheric pollution and smoke abatement, (vi) domestic drainage, sanitation and plumbing, (vii) sewerage and sewage disposal, (viii) building construction, (ix) public cleansing and (x) special premises: factories, workplaces, shops, canal boats, temporary buildings, lodging houses, offensive trades.

These subjects are clearly considered and described with much detail which has been well chosen. There are many useful illustrations and good lists of references. The book is pleasantly readable and well produced. It is likely to be of much interest and value, particularly as a reference book, to public health inspectors and others concerned with the subjects included in this volume. *M. E. Delafield*

AIR MINISTRY. **Handbook of Preventive Medicine 2nd Edition.** A.P. 1269B. pp. xxix + 418, 72 figs. 1959. London: H.M. Stationery Office. [40s.]

This edition is based on the lines of the first which was published 11 years earlier [this *Bulletin*, 1947, v. 22, 604] and was admirably concise, though it did not cover all aspects of preventive medicine in the Royal Air Force. The present handbook is double the size of its predecessor, owing in part to additions to all and sub-divisions of some of the previous chapters on personal hygiene, water, food and nutrition, environment, conservancy, communicable diseases, and disinfection and disinfestation; and in part to the inclusion of 6 new chapters on the promotion of mental health, occupational health of ground personnel, occupational health of aircrew, toxic substances in relation to the aircraft industry, medical statistics, and radiation hazards (the last has still to be issued).

This handbook is designed to be a book of reference not only for medical officers of the R.A.F. but for all those who are concerned with the prevention of disease and the promotion of health and efficiency in the Service. It is clearly written so that, for the most part, it should be readily understood by laymen. In addition, it deserves study by those responsible for health and hygiene matters in civil aviation generally, especially at airports and in the aircraft industry. In this connexion, there is a wealth of sound advice on working environment including factory hygiene, accident prevention, selection of personnel and their health supervision, industrial poisons, and the problem of noise reduction. The chapters on the promotion of mental health and on the occupational health of both ground staff and aircrew are first class. The book is well illustrated, except for the photographs of water testing apparatus and the absence of any illustrations of water trailers, a thorough knowledge of which is so essential in the field. Chapter 6, on climatology, could with advantage be shortened, as it contains much information not essential to the medical officer. However, Chapter 7, dealing with the effects of climatic heat and cold, is excellent.

The book is in loose leaf form, which will facilitate any amendments and additions as required. The editor, Wing Commander W. B. THORBURN, is to be congratulated on the production of such a complete work of reference on preventive medicine in relation to aviation.

H. E. Whittingham

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